MEDICAL RECORD

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—*Pasteur*

OCTOBER 1948

Vol. 161.

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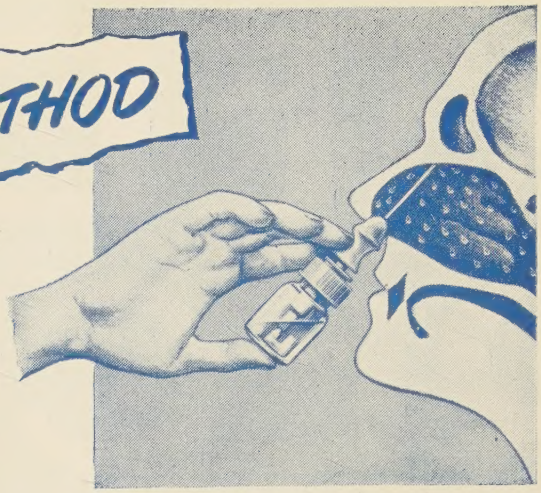

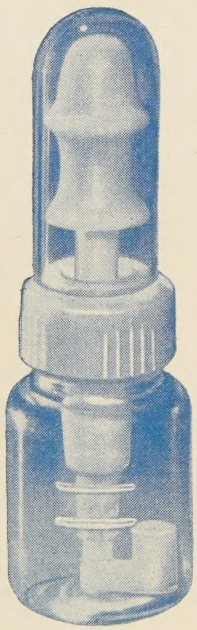

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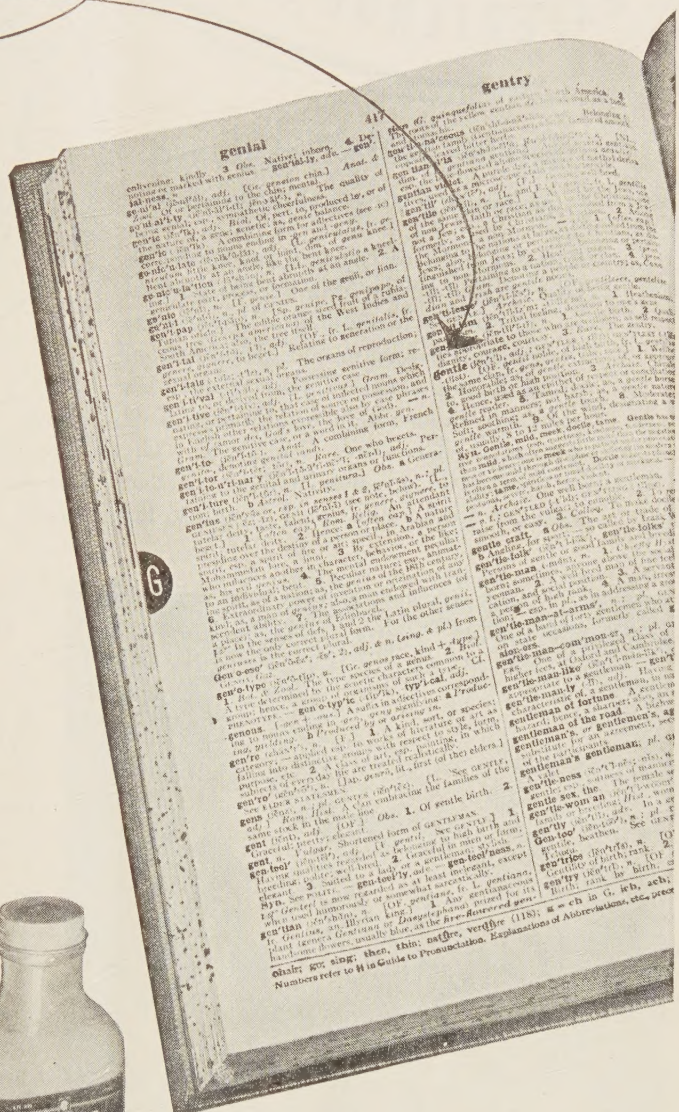

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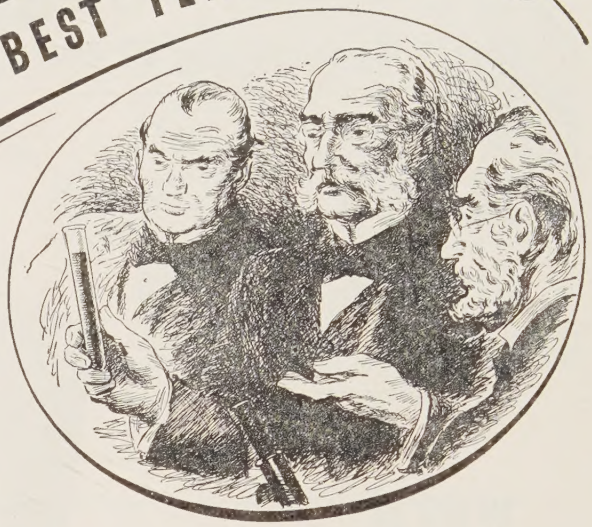

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OCTOBER, 1948

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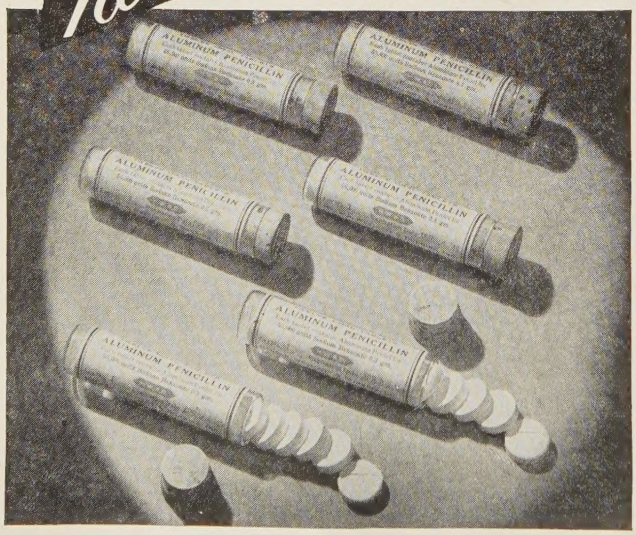

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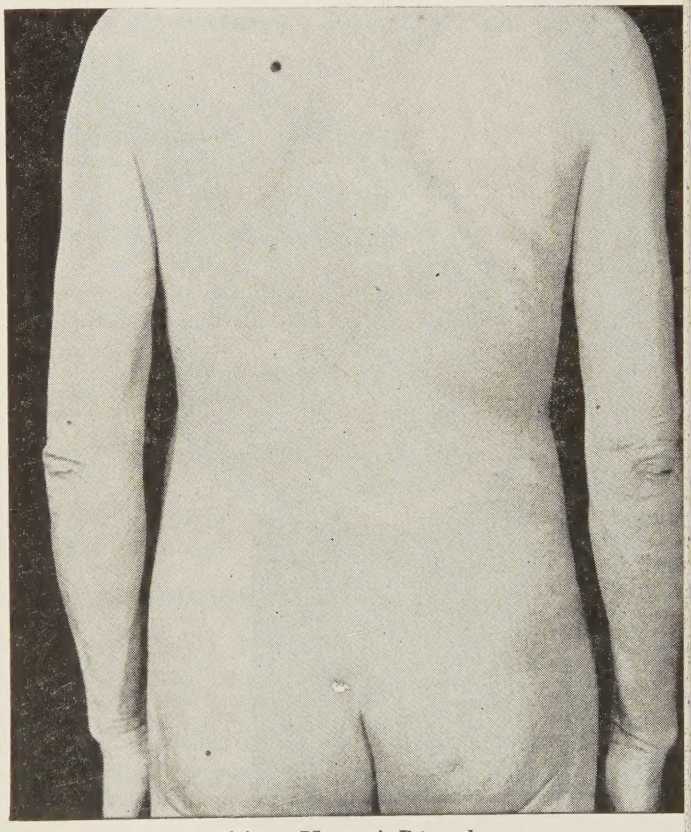

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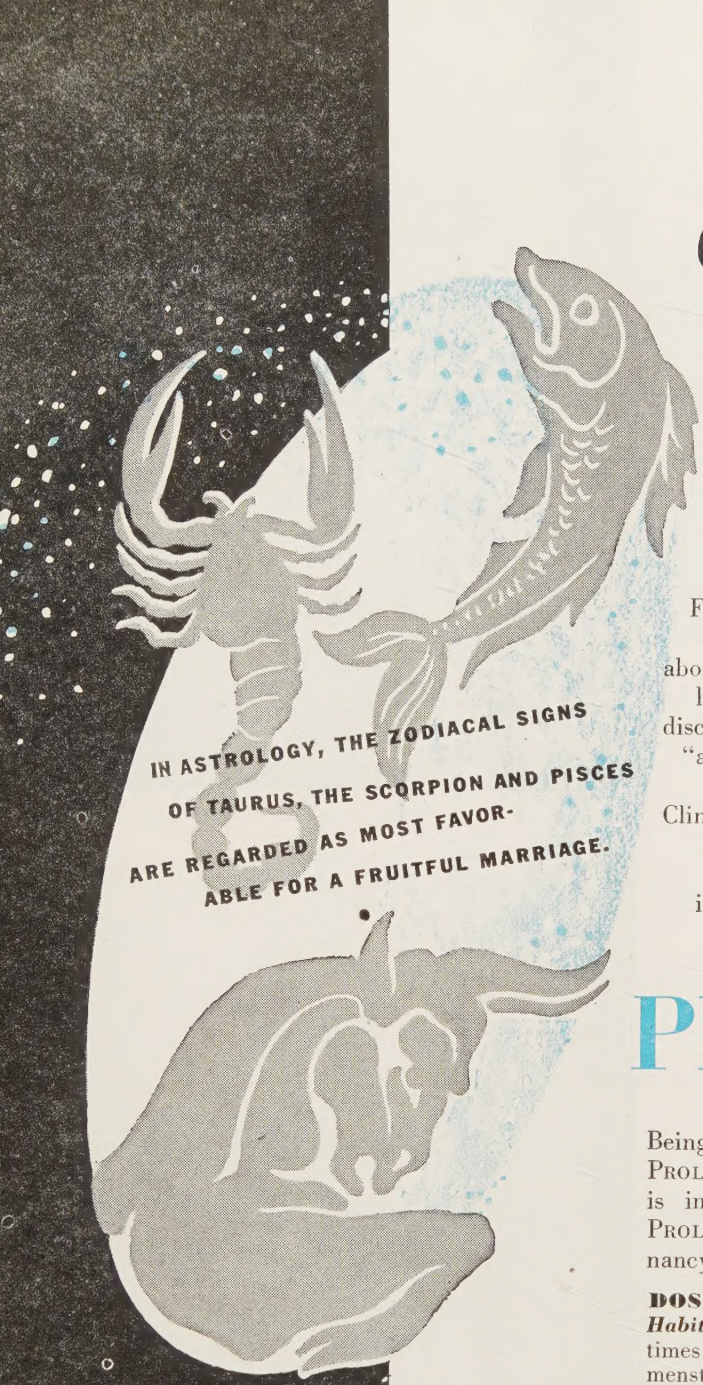

IN ASTROLOGY, THE ZODIACAL SIGNS OF TAURUS, THE SCORPION AND PISCES ARE REGARDED AS MOST FAVORABLE FOR A FRUITFUL MARRIAGE.

good augury in pregnancy

For too long, enchantments and incantations were the only defense against spontaneous abortion. Now, however, prophylactic therapy has been placed on a rational basis with the discovery that the corpus luteum hormone is "a powerful uterine relaxant" as well as being "essential to embedding of the ovum."[1] Clinical evidence has now accumulated which indicates that at least 8 out of 10 habitual aborters may be delivered of viable infants if PROLUTON,* pure progesterone, is injected routinely early in pregnancy.[2-4]

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BIBLIOGRAPHY: 1. Frank, R. T.: M. Clin. North America **25**:607, 1941. 2. Kane, H. F.: Am. J. Obst. & Gynec. **32**:110. 1936. 3. Mason, L. W.: Am. J. Obst. & Gynec. **44**:630, 1942. 4. Krohn, L., and Harris, J. M.: Am. J. Obst. & Gynec. **41**:95, 1941. 5. Soule, S. D.: Am. J. Obst. & Gynec. **42**:1009, 1941.

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New Appointments

Surgeon General Leonard A. Scheele, USPHS, has announced the appointment of *Dr. Cassius J. Van Slyke* as director of the National Heart Institute, under the general supervision of assistant surgeon R. E. Dyer, director of the National Institutes of Health. In addition Dr. Van Slyke will be directly responsible to the surgeon general for coordination of all heart disease activities in the Public Health Service. He will represent the Service in maintaining relationships with professional societies, voluntary agencies and other civic groups who are interested in the progress of the heart disease program.

Dr. David E. Price succeeds Dr. Van Slyke as chief of the Research Grants and Fellowships Division, National Institutes of Health.

Dr. George T. Harding, Columbus, O., has accepted the presidency of the College of Medical Evangelists, Los Angeles. As a member of The Council of the Ohio State Association several years ago and as a member of committees of the Association at various times, Dr. Harding made large contributions to the activities of the organization.

He has also made large contributions to the work of the Columbus Academy of Medicine; to the many groups and organizations throughout Ohio which he has served in an advisory capacity, representing his specialty of psychiatry and neurology.

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Critique

Rutin and related compounds

Waugh and King announced the isolation and identification of vitamin C from lemons on All Fool's Day 1932 and, 15 days later, Svirbely and Szent-Gyorgyi announced the isolation from adrenal glands of hexouronic acid—later ascorbic acid or vitamin C—and demonstrated that it prevented scurvy. Four years later Szent-Gyorgyi and co-workers found that pure ascorbic acid would not relieve all symptoms of scurvy and that impure preparations thereof acted therapeutically in certain hemorrhagic diseases of a nonscorbutic character. This lead them to postulate the existence of vitamin P which helped maintain normal permeability and fragility of the capillaries, but not all the pharmacological properties of the vitamin P substances are yet known, though they do have an antioxidant action toward ascorbic acid and epinephrine. Rutin has some of these vitamin P properties.

Though known long ago, Dr. James F. Couch, of the Department of Agriculture, who isolated it from tobacco and buckwheat plants, first announced this. Rutin stimulates the excised frog heart much as does digitalis; in relatively high concentration it relaxes smooth muscle of excised intestinal strips immersed in warm physiological salt solution; and it has variable affects on the blood pressure.

Rutin's indirect effects are largely attributable to its antioxidant action. It will greatly prolong the relaxation of intestinal strips obtained by epinephrine. It will prevent the death of guinea pigs from lethal doses of histamine if the animals are dosed with it 10 to 30 minutes earlier. Rats receiving rutin are killed by smaller doses of thiourea than are rats given thiourea alone, and they are also killed more readily by exposure to oxygen. Obviously rutin inhibits the rate of tissue destruction of epinephrine. Rutin also increases the survival time of scorbutic guinea pigs receiving suboptimal quantities of vitamin C.

Prayer

A psychiatrist offers this modernized version of the Lord's Prayer for daily use: "Thou Cosmic Movement Continuum! We petition Thee to lend auditory discriminations to these our laryngeal contractions. Lower the threshold of Thy sensory discrimination so that our neuro-muscular-glandular activities do not expend themselves as wasted reflexes. May the alterations in the configurations of our pitifully finite electron-proton aggregates find sympathetic resonance in Thy visual receptors. May the threefold division of our receptor-conductor-effector mechanisms receive to the full the beneficence of Thy cosmic bounty. Bathe our receptors in Thy irradiations of energy-flux, so that our cerebrospinal neurones are ever dynamogenic. May our cortical pathways always keep vigilance over our lower reflexes. And we humbly ask Thee that our endocrines may not hypertrophy, nor our hormones become toxic.

"Preserve us, we pray, so that through all our energy transformation and relative motions, our configurations remain asymetrical. Also, Amative Movement Continuum, may we never hang suspended in delayed reactions; and may the reciprocal innervation of antagonistic muscles never equilibriate itself so that the circular reaction arcs are elicited, or too much damned up accumulate.

"May we likewise suffer not too many inhibitions or repressions. Again we implore Thee, O Sum Total of Electron-Protons, that our inspiration-expiration ratio may never be harmonious with our subvocal speech. Increase our opsonic index; accelerate our reaction time; and thus may we approximate perfect obedience to the energetic imperative. And though we walk through the valley of the shadow of depressed metabolism, may we secrete no useless adrenalin.

"Give us this day our customary calories; forgive us our maladjustments as we overlook other loci their inadequate movements. And, finally, when the negative accelerations of each configuration of movements brings on senescence, and the second law of thermodynamics triumphs over our biochemical reactions, we pray, O Omnipotent Omniscent Cosmic Movement Continuum, that Thou wilt receive each and every locus back into Thy primordial Space-Time Bosom. This we implore in the name of Science! Amen."

Absorbable Sponges and Thrombin

According to the studies of Olwin and Wahl, the use of thrombin with oxidized cellulose is of questionable value, because this extremely acid cellulose inactivates the thrombin. On the other hand, the gelatin sponge, impregnated with thrombin solution still remains efficaceous Personally, I prefer the fibrin foam sponge soaked in thrombin for cases in which other methods (sutures, etc.) fail to secure adequate hemostatis because such sponges are made from fractination of human blood and are homologous, non-reacting, and suitable for use in the human body.

Fractures of the Mandible

When teeth are present these are used to wire the fractured bony segments together and maintain them in proper position. When no teeth are available for this purpose, Stuart Gordon has obtained very satisfactory results by means of interosseous wiring of the bone fragments. Through an incision below the mandibular line the site of the fractured jaw is identified and dissected free. Then two holes are drilled on each side of the fracture line and stainless steel wires are then passed through these openings and ligated to approximate and immobilize the fractured jaw. The method is an excellent one but cannot be used, of course, if acute infection is present.

Too many food producers? *Nature,* London, for July 20, 1929, commented on U. S. reports that this country had too many farmers. This resulted in considerable overproduction of farm commodities and that was just before the big bubble burst, but agriculture had already had a depression of several years duration. At the time the U. S. had about 6½ million farmers, but only a small fraction were efficient, uptodate, prosperous, and contented, there at the top of prosperity. Only about 800,000 had taken full advantage of what was modern agricultural technology at that time.

Overproduction at a low price level plagued the American farmer. Meanwhile Sir Daniel Hall was saying that the average consumption of food and raw materials derived from the land by white peoples required 2 to 2½ acres per head, that the world's white population was increasing at a rate of 5 million annually, that this meant cultivated land must increase annually by 12½ million acres—or that greater yields must be derived from existing acreages devoted both to plants and to animals—for there were no new acreages worth opening up!

Tobacco is a filthy weed The Board of Temperance, Prohibition, and Public Morals of the Methodist Episcopal Church said, in April 1929, that the American tobacco trust was a conscientiousless baby killer because 60 percent of all babies born of cigarette-smoking mothers died before reaching the age of two, primarily attributable to nicotine poisoning. Dr. Charles L. Barber was credited with this statement which no scientific research even as yet justifies; this man was Chauncey L. Barber who belonged to the American Association for Medico-Physical Research, whatever that was, and the *Jour. Am. Med. Assn.,* July 13, 1929 said it was a fake.

Pierre Schrumpf-Pierron M. D., in his *Tobacco and Physical Efficiency,* 1927, reviewed the entire medical literature on this subject and printed a bibliography of 70 pages. He concluded that "smoking . . . by women has no apparent influence over the functions of the genital system." He did not mention anywhere that nicotine from smoking mothers poisoned their babies.

Papillary Cystadenolymphoma This is an encapsulated, benign tumor, occurring in the region of the parotid gland in elderly people. Microscopically, the diagnosis is established by presence of cystopapillary and epitheliodenomatous tissue in one portion of the tumor side-by-side with other tissue almost identical with that of a lymph node. K. G. Tillinger recently reported nine such cases, though this lesion is undoubtedly very rare.

Stomach emptying "The rate of emptying of the stomach increases progressively from early digestion until the process is complete. It depends on progressive relaxation of the pars pylorica of which the sphincter is the most efficient segment. The mechanism of control does not appear to be a specific stimulus to relaxation of the segment by free hydrochloric acid or the products of digestion. Rather does the activity of the antrum seem to depend on its irritability, and, in these studies, on the stimulating action of raw protein to vigorous tonic and peristaltic contraction. With the gradual disintegration of the protein to the products of digestion late in the first phase of the digestive cycle, there is apparently a graded reduction in the intensity of the stimulus to the antrum and consequently a progressive relaxation of the antrum with more rapid emptying. The parallel change of the meal to a fluid state probably facilitates the emptying of the stomach." (Jos. G. McCann, Mayo Clinic, *Am. Jour. Physiol.* August 1929.)

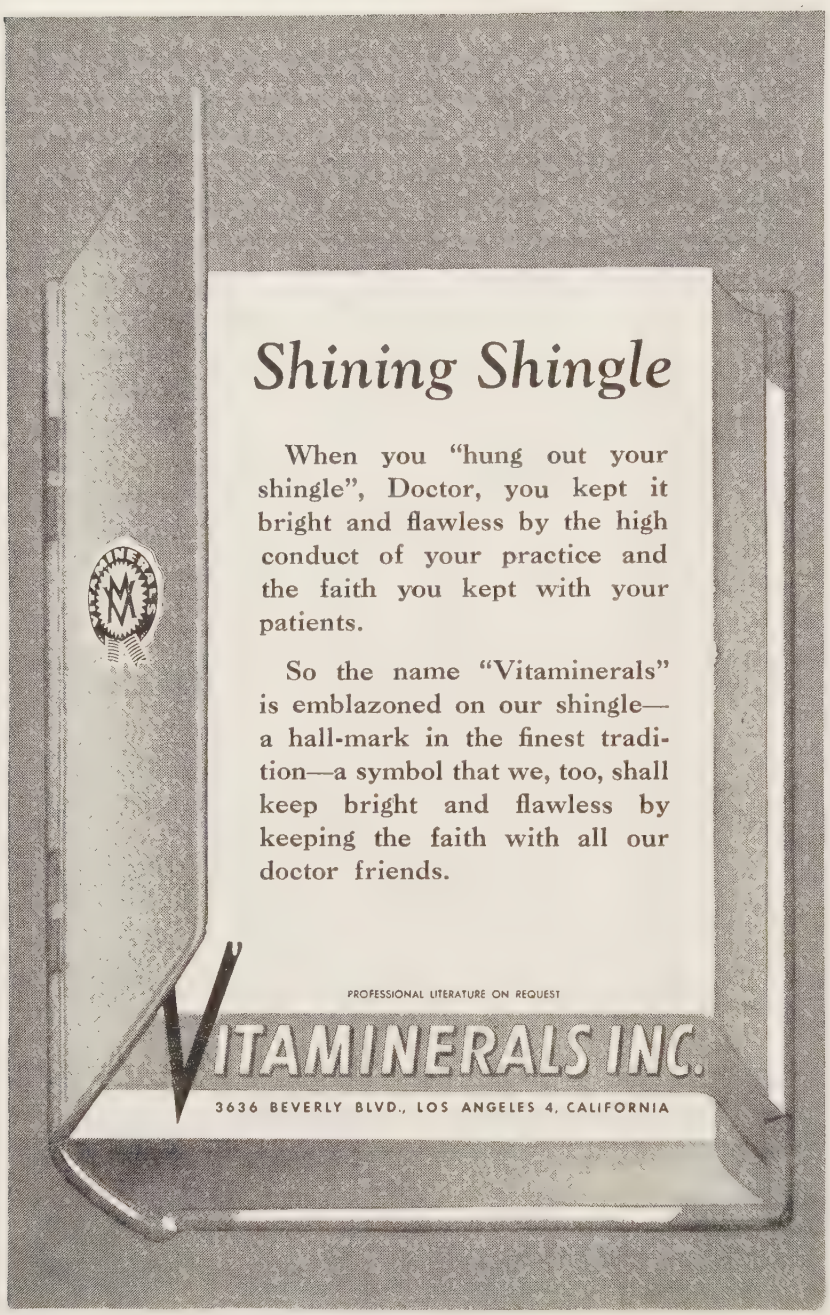
Exstrophy of the Bladder Reid et al. feel that these cases now have a better prognosis since one can utilize the extraperitoneal approach in implanting the ureters into the rectum and they advise that this operation be done before the child is six months old. When cancer occurs in such an exstrophic bladder it is an adenocarcinoma, the authors point out, whereas when cancer occurs in a normally situated bladder the malignancy is very rarely of this type.

Psychic disturbances According to Atthur Grollman in the *Am. Jour. Physiol.* for August 1929, psychic disturbances can very markedly increase the blood and pulse pressure and have an appreciable effect on the heart output, depending on the nature of the individual and the tendency to excitement. All psychic disturbances must be avoided in measuring the cardiac output. Cardiac output may increase 0.9 liter in anger in some subjects.

Cancer of the Larynx L. H. Clerf is emphatic in reminding us that the only safe and satisfactory treatment for this condition is *radical* laryngectomy. We must not try to save the patient's voice or be swayed by cosmetic reasons to conserve bits of cartilage and portions of muscles. To do so simply jeopardizes the patient's life.

Primary Cancer of the Seminal Vesicles This is a rare disease and is often confused with cancer of the rectum or Blumer's shelf tumors. Patients with cancer of seminal vesicles have this palpable mass just above the prostate gland, hematuria, urinary frequency, and dysuria. Unfortunately, the prognosis is uniformly bad because radical excision is impossible and the only therapy possible is palliation.

Mesenteric Thrombosis E. D. Engelman reports the successful use of anticoagulant therapy (instead of surgery) in the case of a weak and elderly man found to have mesenteric thrombosis upon exploratory laparotomy. When the bowel is still viable such a conservative measure may be partially justified, especially when the patient cannot stand the shock and consequences of intestinal resection.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The "petechiometer," works on the principle of negative pressure (suction) applied over the biceps. After the application of suction for a period of only 60 seconds, an accurate petechial count can be made through a magnifying lens incorporated in the head of the instrument.

Altogether, only two minutes are required for the entire determination, whereas positive pressure methods require as much as 20 minutes time. The "petechiometer," which takes up no more room than a 30 cc. syringe, is available in all Rexall stores.

Eponyms

An early Greek, one whose work is closest to that of Hippocrates, the clinician, is Aretaeus, born in Cappadocia about the second half of the first century (30-90 A. D.). He lived toward the close of the reign of Nero. Aretaeus was known to have lived in Alexandria, was a good clinician and an attractive medical author. He described symptoms accurately, and the descriptions are readily recognized. He gave excellent accounts of pneumonia, pleurisy with empyema, diabetes, tetanus, diphtheria, the aura of epilepsy and very full accounts of various types of insanity. The eponym we have is *Elephantiasis Aretaei*, or nodular leprosy.

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VOL. 161 OCTOBER, 1948 WHOLE NO. 2788

COMPLEMENT FIXATION REACTION

By M. GERUNDO, M. D.
Hilo, Hawaii

History

Of all the tests that the minds of bacteriologists have been able to devise, this is the most fascinating and perhaps the most obscure of all. With the great expansion of research, with the legions of experts trying to wrest a secret out of a test tube, the reaction has not advanced yet from the stage of witchcraft. If one would have dared to make diagnosis of an unmentionable disease by mixing in a test tube human serum with the saline extract of liver of a fetus born dead, the fluid part of rabbits' blood, fed or, scientifically speaking, injected with the blood of a sheep, the blood fluid of a poor innocent virgin animal, like a guinea-pig and finally the blood of a young healthy sheep, he certainly would have risked his life in days gone by. Where is the difference from the cave witch of the middle age looking at the viscera of a recently slain animal at the light of a candle or an oil lamp? Still the Bordet-Wassermann test is a scientific achievement, born of scientific witchcraft.

As it is well known in the general history of bacteriology, Bordet demonstrated the lysis of bacteria by introducing an indicator system. As lysis takes place only in presence of complement, he introduced sensitized sheep cells into the system and watched for the lysis of the cells. If the complement had been already removed by the lytic antibodies the sensitized cells failed to undergo hemolysis.

Bordet and Gengou in a long series of experiments demonstrated very brilliantly that complement fixation was a general phenomenon and that through the use of an indicator system, like the sensitized sheep cells, it could be applied to the diagnosis of many bacterial diseases.

The history of the Bordet-Wassermann reaction is linked with that of bacteriology and immunology so intimately that we would risk at this time to repeat what has been already said about it in other chapters.

It is granted now that Bordet was the first one to apply his complement fixation to syphilis. Because of the inability at the time of culturing spirochetes, he used saline extract of chancre as an antigen. But, as he was still under the influence of strict immunological procedures, he concluded that the reaction was unreliable because an extract of normal organ that he used as control, had also fixed the complement. Definitely, the reaction was not an indicator of a true immunitary process, as he had conceived it for his working hypothesis. He had discovered a new test for syphilis, but he discarded it, because it was not conforming to principles.

The first report of application of the Bordet-Gengou's reaction to syphilis came from Wassermann who, of course, was less scrupulous in scientific matter than Bordet. It is very doubtful that Wassermann used any control of normal organs, as he stated that normal organs did not fix complement. When other authors pointed out to him that extracts of normal organs acted in the same way as extract from syphilitic liver, he finally had to concede that this was true.

The theory of interaction between antigens and antibodies was still fresh in the minds of these early authors. Therefore, they endeavored to demonstrate that fixation took place only in the presence of organs which contained a large amount of spirochete. Wassermann held that non-syphilitic organs were not antigenic, but in view of what we know now about the specificity of organ extracts we can doubt his conclusions.

It must be recalled also that from a strictly historic point of view an Hungarian author, Lazlo Detre, applied the Bordet-Gengou complement fixation to human syphilitic sera even before Wassermann. However, the irony of history sometimes relegates some great pioneers to obscurity. In a way, Fame is a blind goddess who picks up her favorites by the gentle touch of her unguided finger.

If anyone deserved the least to give the name to the reaction, this one was Wassermann.

The progress of the reaction did not have to wait very long. Through the efforts of Levaditi and Marie, Landsteiner, Muller and Poetzl, it was found that normal organs will serve just as good antigens as syphilitic organs and that alcoholic extracts were far superior to watery emulsion. The discovery again threw doubt upon the specificity of the reaction itself, but the test had been already accepted universally. There was no way to discard it for not conforming to principles, but there was no other alternative but to understand the mechanism of the reaction and to improve the technique. The various decades of activity in this field have improved the test and given rise to innumerable modifications, but, like in many other biological problems, have contributed very little to its elucidation.

The history of the Bordet-Wassermann is fascinating, but it has been presented here only in a very sketchy fashion. The reader is gently asked to read the various good monographs available on the subject.

Mechanism of the Bordet-Wassermann Reaction

As originally planned, the mechanism of the Bordet-Wassermann reaction is based upon the introduction of two systems of antibodies, both needing complement for their action. Without recurring to any old conception of immunity and siding with this or the other theory, we can simplify the principle schematically in this way:

ANTIGEN (extract of normal organs)	SHEEP CELLS (representing the antigen)
ANTIBODY (supposed to be present in the serum of syphilitic patient) (called also reagin)	ANTISHEEP HEMOLYSIN (antibody artificially produced in rabbit)

The second system is simply an indicator; the worker may choose another system at his will, depending upon the availability of the material. A glance at the schematic representation of the reaction will show us that both systems belong to the so-called third order of antigen-antibody complexes; therefore, neither one will act without the addition of a hypothetical neutral substance present in the serum, called complement or alexin. Complement is fixed, that is, firmly bound, only in the presence of an antigen-antibody complex; the presence of either one alone will leave complement free.

In the classical Wassermann reaction the antibody or reagin in the serum of syphilitic serum combines strongly with the antigen and the complex formed binds the complement. By allowing a certain time during which all or part of the complement has been bound, depending on the amount of reagins present in the serum, a second system is then added to the reaction. The new antigen-antibody complex will result in dissolution of the red cells, only if free complement is present in the test tube, but no hemolysis takes place if the first antigen-antibody complex has bound all or almost all the complement available.

Diagrammatically, we can represent now all the various combinations which may take place:

I

ANTIGEN — SHEEP CELLS

Complement — No Lysis

REAGIN — HEMOLYSIN

II

NO ANTIGEN — SHEEP CELLS

Complement — Lysis

REAGINS — HEMOLYSIN

III

ANTIGEN — SHEEP CELLS

Complement — Lysis

NO REAGIN — HEMOLYSIN

IV

NO ANTIGEN — SHEEP CELLS

Complement — Lysis

NO REAGIN — HEMOLYSIN

V

NO ANTIGEN — SHEEP CELLS

Complement — No Lysis

NO REAGIN — Free — NO HEMOLYSIN

The amount of complement present in the serum of animals is variable, not only from species to species, but also in the same individual from time to time. Therefore, to obviate errors in the technique, the early authors applied the reaction on serums which had been deprived of their complement, by heating at 56°C. Complement is heat labile and is completely inactivated by heating at 56°C for 30 minutes. The procedure which employs inactivation as a prerequisite for the test is called inactive serum method and is still considered as classic, in contradistinction to the newer methods or so-called active serum methods which employ fresh unheated serum. We will return to this point later.

From the foregoing discussion, it is easily understandable that excess of one or the other component of the reaction may cause great variation in results. To avoid such possibility, the need has arisen to determine beforehand the amount of complement needed to give a positive reaction. Should any free complement still be present after part of it has been fixed by the antigen-reagin complex, the excess may well serve to activate the second system of sheep cells-hemolysin, thus creating the possibility of a false negative reaction.

On the other hand, if the complement added is weak or below a certain optimum, it may be partially fixed by the first complex or absorbed by either the serum or the antigen and the remainder may be insufficient to produce complete hemolysis. This error may cause a false positive reaction, which may have a perturbing influence upon both the doctor and the

patient. It is therefore imperative that the test have all the necessary controls and preliminary titrations, to assure a reasonably specific reaction and to prevent errors. The components of the test which need to be titrated and controlled are antigen complement, and hemolysin. They must be added to the reaction in the proper dilution, as established by preliminary trials.

The techniques of titration are varied and numerous, but once the basic principles of the reaction are understood, every one of them is easily mastered and can be tried out with success, contrary to the common teaching that only one standard technique should be followed in order to avoid errors. What matters in the test is not to familiarize oneself with dilutions and figures, as not given by the various authors but to understand the principles of the reaction and present-day theories. Standards in science are static and they tend to restrain, rather than to foster progress. It is true that good housekeepers may cook a good meal by following the cook book method, but if they do not know the nature and quality of the ingredients, they run the risk of preparing a meal which is not just fit to eat.

Diagrammatically, we may present one of the most common errors in this way:

I

ANTIGEN — SHEEP CELLS

\ Complement / Lysis

Fixed Excess

/ \

REAGINS — HEMOLYSIN

II

ANTIGEN — SHEEP CELLS

↑ Complement

loosely bound or partially absorbed — Insufficient → No Lysis

NO REAGINS — HEMOLYSIN

Is the Wassermann an Indicator of an Immunitary Process?

Although great strides have been made in the technical improvement of the test, there is still little knowledge of the inherent mechanism and still less is known about the relation of the test to immunity. As we understand at present the mechanism of immunity, antibodies are formed in the organism as a defensive mechanism against living agents of disease. As disease progresses and the organism is the victor in the struggle for survival, we would expect the blood to contain large amounts of antibodies for that particular injurious agent.

In syphilis direct observation of the immunitary process was not possible because of the inability of culturing the spirochetes. However, when such culture was made possible by improvement in bacteriologic methods, it was soon discovered that the spirochetes did not make such good antigen for the test, as it had been anticipated, and that the extract of normal organs was a far superior antigen. It was then assumed, and so far it must be considered only as rationalization of the failure, that the cultivated organism has no serologic or immunologic relation to the virulent strains, because of changes in structure brought about by the artificial culture (rough variant).

But, of course, this still does not explain the fact that with recovery following treatment, the serologic reaction becomes negative. In a true immunitary process, we would expect that not to be the case. The titer of antibodies should be at its maximum and the serological reaction strongly positive. This is not the case for the Wassermann, which, to a certain extent, is more a direct measure of the intensity of the infection rather than of the organic response. It is known that chancre fluid may fix complement; and that complement fixation does not always parallel the trend of other antibodies, like agglutinins and precipitins, and may be positive at a time when no direct immunity has been established.

This is true not only for syphilis, but for other diseases as well. Blackfan has demonstrated it for lymphocytic choriomeningitis, in which the complement fixation is present much before the appearance of neutralizing antibodies in the blood of patients.

It is still a matter of considerable doubt whether complement is involved in immunitary processes at all, as animals which have a good supply of complement would then be either better prepared for defense against disease, or the more likely to develop good immunity. We associate complement with antibodies of the third order because these cannot act but on fresh serum, but we overlook the fact that heat disturbs the colloidal equilibrium of the serum and therefore a normal behavior. We entirely disregard the fact that many properties of fluids and cells are not demonstrable after heating above the optimum for normal function. Complement follows exactly the same line as any other biological activity; it is preserved by cold, destroyed by heat.

We must consider the point of view that Tr. pallidum is a histiotropic agent like viruses and, to a certain extent, tubercle bacillus. There, perhaps, we may find a rather interesting suggestion that the reaction is only a manifestation of allergic nature. Because of the histiophilic nature of the spirochetes, it is possible that broken down products are able to fix the complement, not only in vitro, but probably in vivo.

Some studies carried out by the author several years ago on natural hemolysis show that the hemolytic index is low in syphilis and that anticomplementary reactions, that is, fixing of an excess of complement, are definitely more common with syphilitic serums. This fact would tend to demonstrate that there is an X substance, called reagin, which has nothing to do with immunity, but is very avid for complement. Recent incomplete studies by the author, as yet unpublished, may seem to show that complement is decreased in syphilis, perhaps in relation with the disturbance of serum proteins. With recovery, a normal equilibrium is reestablished and this is followed by disappearance of complement fixation.

Whether the process may be compared rather to tuberculin or atopic sensitization, where the reaction disappears when desensitization takes place, or immunity is built up, is just a matter of speculation

which cannot be discussed in a text book.

Eagle and Hogan support the thesis that the serologic reaction is induced by antibodies. Tests carried out on absorption tend to demonstrate that cultured spirochetes remove all the reagins from the serum, and that immunization of rabbits with tissue lipoids induce agglutinins and complement-fixing antibodies for spirochetes. However, Black-Schaffer and Rohsan, in a study of relation between serologic and autopsy findings, concluded that increasing activity of the disease is associated with an increasing frequency of positive blood tests, but that there was no correlation between anatomic lesions found and reversal of serologic reactions.

Kolmer, Kast and Lynch conclude that absorption of human syphilitic sera with spirochetes removes the complement-fixing antibody for the spirochetes, but does not remove the reagins in the Wassermann reaction.

Complement undoubtedly seems to play an important essential part in the bactericidal action of serum as proved by the work of Dozois, Seifter and Ecker, but whether there is a similar relation to the serologic reaction in syphilis only new knowledge of the intimate mechanism will tell, by throwing some light on this debatable question. At the present time we can simply accept the Bordet-Wassermann as an application of the complement fixation technic to the detection of reaction between lipoid antigen and serum reagins and be satisfied with the diagnostic advantages that such reaction offers.

Various Components of the Reaction Complement

It would be impossible to enter the controversy raging as yet about the nature of complement. There is a large extensive literature on the subject and space does not allow going into detail.

The various theories of multiplicity of complements or of specificity have now only an historic value. Its origin is still a matter of dispute, as the original idea of being a product, or a by-product, of leucocytes did not hold true. It is essentially proteic, but one fraction may be a phosphoprotein and still another a mucoprotein. It has been found that the complement is linked with globulins and albumins and that any agent which disturbs the equilibrium of protein will definitely destroy the complement. There is no species-specific complement and no increase during active immunization.

The first study on the complex nature of complement was that of Ferrata who demonstrated the presence of two pieces by dialysing the serum. Soon afterwards, through the studies of Coca, Gordon and Ecker, Pillemer and Heidelberger the complement has been found to consist of at least four component parts which, however, may not exist in the same proportion in the serum of all animals. The fraction which is precipitated with the euglobulins has been called midpiece, it being the most important in binding the antigen-antibody complexes; the part which remains in the supernatant fluid has been called the end piece, and most of it remains free in the reaction. These two parts are inactivated by heating the serum at 56°C. Coca discovered a fraction which is absorbed by yeast cells and is mostly heat-stable; and Gordon, Whitehead and Wormall reported a fourth fraction which is also heat stable but is inactivated by ammonia. Quick and others have pointed out similarities between prothrombin and complement, possibly with some convincing evidence. It must be added that both originate from the liver and that patients deficient in prothrombin are also deficient in complement.

Ecker advanced a very suggestive theory that complement resembles certain hydrolytic enzymes possessing a —SH group.

Complement is very unstable; it is easily destroyed by heat, storage at room temperature, prolonged shaking, proteolytic ferments, ether, chloroform, alcohol, bile salts, soaps, filtration through Berkefield filters, low pH., etc. It can be preserved for at least one year by freezing and storage at -35°C., according to Seifter, Pillemer, and Ecker. Various methods of preserving complement for a limited period of time have been proposed and for a small laboratory perhaps the best practice is that of using hypertonic salt solution to which boric acid or glycerol has been added. However, there is now an extended supply of dry complement available commercially which has definite clear advantages over old methods of preservation.

The author carried out a series of investigations on the nature of complement. Lipase enhanced the activity of complement, but, however, when added to complement inactivated at 56°C and to old complement which had lost its activity, did not restore its activity. The addition of cystine, glutathione, and tyrosine was without influence upon the activity of complement. Although lipase itself has the property of increasing almost twice the complementary activity, it was unable to replace complement entirely. From this work no definite conclusions could be drawn that complement is an enzyme or a complex of enzymes, but there are many evidences which seem to show connections between enzymatic action and hemolysis by complement and hemolysin. No definite link was discovered between the -SH groups and the complement.

Hemolysin

The system most often used in the Wassermann reaction is the antisheep hemolysin. However, other systems have been used in the past, depending on the availability of animals. The author has used quite often the anti-human hemolysin which was introduced by Noguchi. There are some drawbacks in this system, and chiefly, the inability to obtain a hemolysin which would work at high dilutions. It is for this reason that antisheep hemolysin has become now rather universal and gives very good results, particularly when the titer is very high.

It is known that serums of various species possess natural hemolysins against red cells of other species. The human serum contains hemolysins against sheep cells, which sometimes may have some influence upon the reaction. These natural hemolysins are different from the immune bodies

produced by artificial means.

When human blood is injected into the rabbit, for the production of anti-human hemolysins, the animal immune serum acquires also the property of hemolyzing sheep cells. This is particularly true when Type A blood is injected. These natural or atypical hemolysins are called heterophile, whereas the term isophile is left for those hemolysins which are specific for the type of cells injected. Heterophile hemolysins for sheep cells may be also produced by injection of bacterial cells, particularly enteric bacteria, like Salmonella, Eberthella, Shigella.

Some experiments carried out by Gerundo and Gold, have shown that amylase is capable of hemolyzing sheep cells in presence of complement. The addition of calcium chloride enhanced the activity of hemolysis perhaps through action on amylase. These experiments prove again that the whole system of hemolysis is very much like that of enzyme and that there are definite connections between the two, which may lead finally to the understanding of the phenomenon.

Natural hemolysins are decreased in syphilitic serums, according to past investigations by the author. By conducting titrations of the hemolytic index in normal and syphilitic serums, he found that those serums which showed stronger fixation showed also a lower hemolytic index.

Neisser and Wechsberg observed that when varying amounts of hemolysin are mixed with a constant amount of complement and antigen, there is no hemolysis until the optimum amount of hemolysin has been reached. But, if an excess of hemolysin is added, hemolysis may fail to take place. This phenomenon, known as the Neisser-Wechsberg phenomenon, is observed also in other antibody-antigen complexes, like precipitins, agglutinins, Wassermann antigens-reagins in the region of excess of either one. This is better called the prozone phenomenon.

To a certain extent, hemolysin may replace complement. Ronchese worked out a table of optimum proportions. The author studied the same problem and worked out a similar table which differs but slightly from that of Ronchese.

TABLE OF RONCHESE

Complement	3	2	1	½	⅓	1/5
Hemolysin	⅓	½	1	2	3	8

TABLE OF GERUNDO

Complement	4 (3)	3 (2)	1	¾	1/5
Hemolysin	½ (½)	¾ (¾)	1	10(8)	15(12)

Antigen

The number of antigens which are now available for the Wassermann reaction is large and, of course, they cannot be mentioned and described here. One of the most important points in using tissue extract is that the antigen must have great sensitivity, but must not fix the complement by itself or hemolyze cells.

The extract which replaced the original Wassermann watery infusion was prepared with alcohol. Although the alcoholic extract proved to be a better antigen than the original watery extract, it is now known that it is quite insensitive. A more involved process has been elaborated, by means of which very good highly sensitive antigens may be prepared, which show practically no anticomplementary activity.

Noguchi introduced first the acetone insoluble antigen. Following his original work, many modifications have taken place which are too technical for detailed description here. The reader is referred to the work of Eagle for more information about the subject.

The organ which is now more in vogue is beef heart, which yields a very good antigen, but it must be kept in mind that the so-called Wassermann antigen may be found in practically every organ of all kinds of animals and the active principle may even be present in alcoholic extracts of microorganisms. The same process of extraction, however, will yield Wassermann as well as Forssman antigen and this last antigen may definitely be a hindrance in the test. Therefore, attention must be paid in the selection of animals to avoid using those which possess Forssman antigen.

It has been found that various substances may fortify the antigenic properties. Among these substances, cholesterol gained the reputation of being a fortifying agent on purely empirical grounds and has maintained its popularity. Cholesterol forms microscopic crystals when in aqueous solution, which furnish a surface for the absorption of the antigen and for the antigen-antibody reaction. Other fortifying agents are lecithin and phenol, but the mechanism of action of both is still pretty obscure.

The injection into the rabbit of so-called Wassermann antigen, tissue extracts, antigens with tumor specificity, antigens from animal bacteria and parasites, antigens from spirochetes and trypanosomes, when accompanied by a protein and sometimes other inert conveyors may evoke the production of antibodies of the Wassermann type. Tuberculous infections and to some extent malignant growth may evoke the same type of antibodies. None of these antibodies exerts a protective mechanism, a point which has been already discussed in the chapter on the relation of Wassermann reaction to immunity.

For a time it was believed that spirochetal antigen would replace organs extract, but it has been proved in various surveys on evaluation of antigens that the spirochetal antigen has much less sensitivity than extracts from organs. However, serums prepared by injection of spirochetes have proved to be specific for spirochetal extracts. It is possible that the difference in sensitivity is definitely due to difference of antibodies and that antibodies showing in presence of spirochetes are of the protective type. This point is far from clear and waits further work for elucidation.

Pangborn has extracted a new phospholipid from beef heart which seems to be essential to reactivity in the serologic test of syphilis. She has named it

cardiolipin and has found that its activity is similar to the phospholipids extracted from bacterial cells.

Further study on the nature and chemistry of cardiolipins may possibly throw additional light on the mechanism of these organ extracts in complement fixation. Up to now we must keep in mind that the lipoid Wassermann antigen has nothing in common with the true antigens and that the so called antibodies with which it is supposed to enter into union have no relation with the protective antibodies which are supposed to exist in response to infection. Reagins remain hypothetical substances which may be elicited by various means and by injections of haptens but have nothing to do with the establishment of immunity. Reagin titer is not a direct expression of the degree of immunity or of resistance to the infection. If such were the case, one might expect the titer to be very high in long standing latent syphilis and rather low in early syphilis. Instead we have the paardox that the reagin titer is higher in early syphilis and sometimes low in latent syphilis. It is true that Moore and Eagle explain this phenomenon by stating that in early syphilis many more treponemes are broken down by the host's own defenses, concomitant with spontaneous healing of the lesions, and that the reagin titer in human beings falls if the syphiloma is excised. It may be that the behavior of reagins during the treatment and after offers an expression of the patient's immunity.

Sherwood, however, doubts the antibody nature of the syphilitic reagins while Kline goes so far as to suppose that reagins should be present in the body since the first day of appearance of the lesion.

This matter, too, seems to be left over for solution to a new generation of scientists.

Specificity of the Reaction

The test is remarkably specific, therefore, its popularity has increased to a point of being used in various surveys to detect potential sources of infections, and latent syphilis. As the specificity has increased, soon errors and possible sources of misinterpretations have developed.

It is true that, given the widespread use of the reaction the percentage of false positive reactions is only about 1 :4000, but such possibility should be kept well in mind. Yaws, leprosy, malaria, infectious mononucleosis have been often cited as yielding a percentage of false positive from 20 percent for infectious mononucleosis to an 80 percent for leprosy and almost 100 percent in some forms of malaria. Dongeloh points out that non-specific reaction in malaria may be eliminated by diluting the patient's serum with normal serum instead of saline.

Moore and Eagle have pointed out that false positive reactions can be obtained in diseases, like upper respiratory infections, various infections, vaccinia, rat bite fever, typhus, and occasionally in normal individuals who have no manifestations whatsoever of any disease. It is well to remember this fact because a positive reaction carries the threat of social stigmas and may have profound influence upon the patient himself or the victim of such a serologic error. In such instances, perhaps the quantitative method of reagins titration should be resorted to, because false positive reactions have usually low titer.

Even in view of such non-specific reactions, Eagle believes that the reaction in syphilitic persons is due to antibody present in the blood and that normal persons may contain substances with qualitatively similar effects on the lipoidal suspensions called Wassermann antigen. The aggregation of these lipoidal suspensions may give clumps indistinguishable from each other in both cases of true antibody-antigen complex and of normal serum. This hypothesis seems entirely speculative and, while it cannot be denied that two different phenomena may give rise to similar effects, it cannot be accepted without further experimentation.

Occasional positive reactions are obtained in tuberculosis, Boeck's sarcoids, and meningitis. But on the other hand, occasional false negative reactions which are not depending on technical errors may be just as misleading as the false positive ones. Krakauer has pointed out that true paretics with positive colloidal gold curve or positive or negative Wassermann have shown negative findings in the spinal fluid.

One source of error must be mentioned. Diamond points out that occasionally guinea pig serum may give non-specific fixation of complements.

Difference Between Active and Inactive Methods

The active methods, originated from early work of Hecht and Levaditi are usually criticized without reason as extremely sensitive and unreliable, but it would rather appear that they gain in simplicity and reliability because of the elimination of so many different reagents and of heat inactivation. Reagins are of three types:

1. thermostable;
2. thermolabile;
3. phenothermic, which appear in the serum only after inactivation ot 56°C.

The first ones will be present in both active and inactive serum, the second ones will disappear from the inactivated serum and the last ones will appear only with inactivation. Many flocculation methods which show a certain sensitivity are based upon the appearance of this last type. All these reagins are not present always in the same proportion in every syphilitic serum and, particularly during treatment and in cases of latent syphilis or neuro-syphilis, the thermo-labile reagins are the only ones to persist longer. They can be detected only by the active complement fixation.

It has been pointed out that some serums contain a high titer of hemolysin which may induce a negative reaction. This can be obviated by making use of gradually increasing amounts of serum and comparing every reaction tube with the control. Other authors have determined the hemolytic index prior to the test itself and have employed the exact amount of sheep cells, as indicated in the preliminary test.

Malaria and leprosy are not likely to interfere with the active serum test. In leprosy, heating produces the formation of pseudo-reagins which will give positive results with the inactive method. A large number of leprosy cases gave no fixation with the author's technique, whereas it gave fixation

when the serum was inactivated at 56°C. Anticomplementary reactions are also less common in active serum methods than in some inactive serum techniques.

Techniques

It will be impossible here to give all the details of the reaction, which are well given in specialized books. We will briefly describe one inactive serum technique commonly used in this country and one active method.

Eagle Technique

Reagents needed:

1. *Antigen:* 50 grams of Bacto-Beef Heart special for antigen are extracted with 250 cc. of pure anesthesia ether for 15 minutes at 37°C. The mixture is filtered and the powder extracted again with fresh ether, for a total of four extractions. After the fourth extraction, the powder is filtered, washed on the filter with 100 cc. of ether, dried, and then extracted for five days with 250 cc. of absolute alcohol. The alcohol extract is filtered, and the moist powder washed on the filter with small portions of alcohol until the volume of combined alcoholic filtrate and washings is equal to 250 cc. The clear, straw-yellow extract represents the antigen, which is then fortified with 0.6 percent cholesterol (6 mgr. per cc. of extract). For use in the test, it is freshly diluted with 80 to 200 volumes of 0.85 percent saline, depending on the titration, and determination of its optimum antigen dilution. In preparing the antigen for daily use the correct volume of salt solution is slowly poured into one volume of antigen.

2. *Complement:* This is prepared by bleeding guinea pig from the heart. Pooled serums are better than serums from a single pig. The complement may be kept for several weeks, if salted (80 mgrs. of NaCl for each cc. of serum, dissolved by shaking) and preserved in the freezing compartment of the refrigerator.

Serum or spinal fluid to be tested:

Serum is obtained by centrifuging coagulated blood. Spinal fluid is used as it is, if clear; otherwise, it must be centrifuged to eliminate red and white cells.

Salt solution:

0.85 percent solution of NaCl in distilled water.

Sheep Cells: Citrated sheep blood or defibrinated blood is centrifuged three times and finally diluted with 0.85 percent salt solution to make a suspension of 3 percent.

Hemolysin:

The minimal hemolytic quantity or unit of hemolysin must be determined prior to the test itself. In the test 2½ units of hemolysin are used. The hemolysin dilution is poured into an equal volume of the three percent cell suspension to form the 1½ percent suspension of sensitized cells which is actually used in the test.

Technic of Hemolysin Titration

Example of reading of hemolysis after	Amboceptor titration*						
	1:1000	1:1500	1:2000	1:3000	1:4000	1:6000	1:8000
Amboceptor dilution, cc.	0.4	0.4	0.4	0.4	0.4	0.4	0.4
3 percent cell suspension, cc	.4	.4	.4	.4	.4	.4	.4
Salt solution, cc.	.8	.8	.8	.8	.8	.8	.8
Complement, 1:10, cc.	.4	.4	.4	.4	.4	.4	.4
½ hour at 37°C.	Complete	Complete	Complete	Complete	Partial	Partial	None

* The following is a simple method of setting up these amboceptor dilutions:

1:1000 amboceptor, cc.	0.4	0.27	0.2	0.13	0.10	0.067	0.05
Salt solution, cc.	0.0	0.13	0.2	0.27	0.30	0.34	0.35
Final dilution of amboceptor	1:1000	1:1500	1:2000	1:3000	1:4000	1:6000	1:8000

Test

Three tubes are needed. Tube 1 is the serum control, containing serum and complement, but salt solution instead of antigen.

	Serum Control	Test	Proper
Whole serum, cc.	0.2	0.2	0.1
Complement, 1:10, cc.	.4	.4	.4
Antigen dilution, cc.	.0	.4	.4
0.85 percent NaCl, cc.	.6	.2	.3

The antigen control (one for the whole series), is set up in a similar way, by omitting the serum and using saline to make equal volume. Complement controls are set up the same way.

The same technique can be used for the spinal fluid, but a larger amount of spinal fluid is needed for the test.

The test tubes are left for three to four hours at 0 to 5°C, after which time they are placed in the 37°C water bath for 30 minutes. Eight tenths of the sensitized cell suspension is then added to all the tubes, which are vigorously shaken and replaced at 37°C for their final incubation of 20 to 30 minutes.

Reading of the results: The antigen controls should be completely hemolyzed. Complement controls should show also complete hemolysis. The serum control tubes should show complete hemolysis. In the test tubes lack of hemolysis means positive complement fixation, complete hemolysis negative complement fixation. There may be all the intermediate steps between complete hemolysis and no lysis, which correspond to doubtful or weakly positive reactions.

A quantitative test can be set up with various dilutions of serum. For details, the reader is referred to the original description.

It must be noted that Eagle, like Calmette and Massol, does not titrate complement. The author is in agreement with such procedure, as the titration of hemolysin is sufficient. In other techniques complement is titrated against hemolysin and hemolysin titrated against complement. This procedure of double titration is awkward, if not incongruous or absurd, as both are unknown components of the reaction and the activity of either one is measured only in relation to an arbitrary amount of the other.

Active Method Gerundo Technique Test

Active serum is diluted 1:2 of 1:3 with saline and distributed in tubes in increasing amounts. By diluting the serum 1:2, only one cc. is needed for the reaction.

The tubes are set in two rows, the first belonging

to the reaction proper, the second to the control. In case of insufficient amount of serum, three tubes can be used, this reducing the amount needed to only six tenths of a cc.

TABLE I
SET-UP OF THE REACTION

	Reaction Tubes	Control Tubes	Reaction Control
Unknown serum 1:2	1 2 3 4	1 2 3 4	
Syphilitis serum			1
Negative serum			1
Antigen, titrated	1 1 1 1		1 1 2
Saline	3 1 1	4 3 2 1	3 3 3 5
One hour in waterbath at thirty-seven degrees			
Sheep Cells 2 percent, 5 percent	2 2 2 2	2 2 2 2	2 2 2 2

(For those who employ a two percent dilution of sheep cells 0.25 cc. of sheep cells are substituted for the amount above mentioned).

Reading After Twenty Minutes

The control tubes should show complete hemolysis at the end of this time. Should the first tube show no hemolysis, the corresponding tube of the reaction should not be read and results should be based only on the reading of the other three tubes of the reaction. If the second control should show no hemolysis, then the results should be read on the reaction tubes corresponding to completely hemolyzed control tubes.

In case all the four control tubes show no trace of hemolysis, add one or two units of hemolysis to all the tubes. By experience it has been noted that hemolysin is more often absent than complement. Sometimes the heterophile hemolysin present in the human blood is scarce and may fail to show activity even in the fourth tube, containing two-tenths of a cc., but, in presence of a small amount of isophile hemolysin, it shows strong synergistic action. After twenty minutes take a reading. If the control tubes show hemolysis, then read the results and record.

If the control tubes show as yet no hemolysis, then complement is not present in the serum, or is very scarce. One has in this case the choice to either repeat the reaction and add one unit of complement to the reaction tubes before the first incubation, or to add complement directly to the tubes. The author has followed this last procedure with constantly good results. Syphilitic sera will give positive reaction even with such an apparently unorthodox procedure.

From a long series of experiments which I have carried out it seems clear that the fixation of complement by antigen-antibodies complexes takes place more promptly than by hemolysin-sheep cells. Therefore, in case of positive serum, the complement will be fixed by the antigen-antibodies with the result that no hemloysis take place, even if the addition of complement takes place after the addition of hemolysin-sheep cells. The presence of cholesterol in the antigen will facilitate the promptness of fixation of complement upon antigen-antibody complex, by its retarding action upon hemolysis.

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THE USE OF RADON SEEDS (TUBULES) IN THE TREATMENT OF BENIGN AND MALIGNANT CONDITIONS*

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Today, it is universally recognized that radium plays an important part in the treatment of benign and malignant conditions. In some cases it is the treatment of choice, in others it is used as an adjunct form of therapy to surgery. Radium, however, is far from inexpensive and because of its long decay period cannot be left within body tissues for the extended periods sometimes required in treating not so readily removable as also inaccessible lesions.

The hope of finding some other means of applying irradiation in such conditions led to prolonged investigations and it was found that as radium decayed it emitted a gas or emanation called "Radon" which possessed the same physical and biological characteristics as radium itself. In contrast with radium, however, radon's activity is short-lived, lasting no longer than about 30 days. Despite this drawback, radon was recognized as a great possible aid in the treatment of cancer.

How to utilize this emanation in a practical plan for therapeutic purposes, was first worked out by Duane (1) in 1914, who found that this gaseous radio-active substance could be piped into small glass capillary tubes. This made it possible to employ radon in treating various local surface lesions or those within the body, because the tubules could be prepared in any length and be attached to a surface or introduced within the tissue itself.

A careful study was made of the rays emitted from these glass tubules and it was found that, while the glass capsules had absorbed the alpha rays, the beta and gamma rays were barely affected. Since the beta rays were known to be caustic and destructive in character, their elimination for ordinary purposes, except in some special instances, was necessary in order to prevent untoward results.

Beta rays are absorbed by certain metal filters, the thicker the metal the greater being the absorption. In order to filter out the caustic rays in the glass tubules, the latter were encased in metal, but as the early filter material used was brass or lead, the tubules thus covered were quite bulky and rather awkward to use. To overcome this Failla (2) in 1926 suggested making radon tubules directly from finely drawn gold tubing of 0.3 mm. wall thickness. This filtered out 98 percent of the caustic rays, obviating any bulky external filtration. These small tubules were called "seeds."

After exhaustive tests it has been found that gold radon seeds, produced commercially, are definitely leak-proof and readily sterilizable by boiling or by steam under pressure and therefore are quite effective for therapeutic use.

Since radon seeds are so readily applicable, they were especially useful in the treatment of such conditions as within the skull, the orbit, the mouth and the pharynx, the larynx, esophagus, stomach, rectum, bladder and prostate. They are also valuable in treating inoperable fixed malignant adenopathy situated anywhere in the body. Because radon seeds are so easily inserted and, if lost, entail hardly any pecuniary loss, this form of therapy is extremely useful and readily applicable to many conditions where surgery is either difficult, inadvisable for cosmetic reasons, or unsafe because of other general abnormal conditions of the patient.

Hemangiomas: The small hemangiomas in newborn children are readily treated by radon seed surface applicators, which permits ambulatory treatment. Small content radon seeds, 0.2-0.5 mc. each, are attached to a small surface lesion on the skin by collodion or adhesive tape and left in place for a specified time for a dose of 50-100 mc. hrs. This will often make the lesion disappear without endangering the tissues or leaving a perceptible scar. In cavernous hemangiomas a few seeds implanted within the tumor will frequently shrink it completely and when proper dosage is applied, no untoward sequalae should follow such treatment.

Skin: Radon seed therapy is very useful for the ambulatory treatment of small skin neoplasms. This method is especially applicable to basal epitheliomas, and can also be used for small limited squamous cell lesions.

The application is easily carried out. The seeds are attached to adhesive and applied directly on to the lesion and left in place for sufficient time to produce the previously determined dose. One or more seeds are used depending on the size of the lesion and the seeds may contain 0.5-1 mc. radon each. A sufficient number is used to administer 50-150 mc. hrs. per square centimeter of lesion, depending upon its size, location and pathology.

A convenient applicator is made of scotch tape surrounded by adhesive tape. The seeds are placed on the transparent scotch tape and attached to the lesion, which is readily noted through the tape. Surrounding this, ordinary adhesive tape is used to firmly anchor the applicator to the skin. After the determined treatment is administered the applicator is readily removed without harming the skin to which it was attached.

In treating residual carcinoma of the skin following irradiation of a bulky tumor mass, radon seeds inserted around the edge results in complete resolution of the lesion and healing. In recurrent lesions of the skin, interstitial radon therapy often causes complete resolution of the lesion.

Parotid: In parotid lesions surgery in most instances is followed by some facial distortion because

* Read before the American Radium Society, Atlantic City, N. J., June 9, 1947.

of the ramifications of the facial nerve throughout the growth, the cutting of which is often unavoidable even under most careful procedures. With intratumoral radon seed therapy, however, nerve injury is rarely encountered.

Lip: Lip keratosis or small neoplastic lesions can very readily be treated by surface application of radon seeds while large bulky tumors respond well to radon seed intratumoral therapy of 100-150 mc. hrs. per cc. when properly applied. Radon seeds are effective in destroying fixed metastatic neck nodes.

Mouth: Infiltrating leukoplakia of the mouth responds well to radon seed implantation. Because of the difficulty of access and the extent of the lesion, when first reported, radon seed implantation is readily applicable for the treatment of malignant lesions of the floor of the mouth and the buccal surface of the cheek.

Lesions of the mucosa of the hard palate, soft palate and uvula are readily controlled by radon seed therapy. Numerous seeds of small millicurie content are interstitially placed throughout the tumors and when carefully done and the dose properly determined, results are superior to those from radical surgery, and the procedure less destructive.

Tonsil: Radon seed therapy is of exceptional worth in the treatment of both benign and malignant lesions of the tonsil. Where surgery is contraindicated, radon seeds implanted directly into hypertrophied tonsils, diminishes the bulk of the hypertrophic tissue and at the same time eliminates the crypts which are the seat of infection.

In malignant tonsils, radon seeds can be readily placed not only within the primary lesion but also in the surrounding tissues and metastatic nodes and, when properly applied, offer a fair measure of control of the malignancy.

Tongue: In the treatment of tongue malignancy radium therapy is today the method of choice. Radon seeds offer a convenient and effective means of reaching all types of lesions wherever situated. Seeds may be implanted directly into the tumor on the surface of the tongue by way of the oral cavity or indirectly through the base of the tongue by inserting the seed implanters through the neck in the midline over the hyoid bone area. This method is carried out as follows:

The skin of the neck is anesthetized over the midline of the hyoid bone and the pharynx anesthetized with a cocaine spray. Selecting a point on the skin of the neck at the midline about 1 cm. above the hyoid bone, a small horizontal skin incision is made about 1-2 cm. in length. Through this opening are inserted the loaded seed implanters which are pushed up into the base of the tongue, the operator's finger of one hand being placed in the pharynx on the tongue to guide the implanters. In loading the seed implanter the tip of the instrument is first dipped into a water-soluble lubricant which holds the seeds in place in the tube, preventing their falling out, until they are inserted into the tumor. The seeds are deposited in and surrounding the tumor at about 0.5-1 cm. apart.

The radon seeds are usually 0.5-1.5 mc. in strength. The number used depends on the extent of the lesion and the dose prescribed, usually about 2-300 millicurie hours per cm. of time. If ten seeds of 1 mc. each are used, each seed gives off 133 mc. hours and a total dose of 1330 mc. hours is given. Smaller seeds produce a proportionate smaller dose. The seeds are filtered through 0.3 mm. gold. Because their radioactivity disappears early, and on account of their small size, these tubules create no future hazard when permanently left in the tongue, and need not be removed.

Larynx: In larynx lesions, radon seed therapy often may control the lesion and prolong life with comparative comfort. Seeds may be inserted directly into the lesion through direct laryngoscopy or through a surgical exposure of the larynx via a laryngofissure procedure.

Lung: Some workers have been able to effect control of some lung cancer cases by introbronchoscopic insertion of radon seeds into the bronchiogenic lesion visible through the bronchoscope. In some instances, following surgical exposure of the lung tumor, radon seeds are implanted directly into the neoplastic mass and surrounding adenopathy. Some favorable effect have been reported.

Breast: Where operation is contraindicated and where a small breast tumor presents itself, radon seed implantation may offer a means of controlling the local lesion. In metastatic breast nodes in the axilla and supraclavicular areas this therapy may control such involvements for some time. Small recurrent lesions of the chest wall following mastectomy may be readily treated by contact radon. The small seed or seeds are attached to adhesive and placed directly over the superficial recurrence, and left in place for the time necessary to administer the prescribed dose. In larger recurrences interstitial seed treatment is used.

Esophagus: Effective treatment of esophageal carcinoma is still being sought. Early cases have responded in but a few instances to radical surgery and radiation has not been very successful in control of this type lesion. However, radon seed implantation directly into the tumor through an esophagoscope, has shown some favorable results.

Stomach: Because carcinoma of the stomach is usually so hopeless, a pessimistic attitude has been adopted regarding its control. Best results are, of course, achieved with early diagnosis and radical surgery, but even in such cases, often at the time of operation, involvement of regional lymph nodes may have occurred. In advanced cases, little can be accomplished by surgery. Sometimes if radon seeds are on hand and are properly placed intratumorally and in the regional involved nodes, they may offer a temporary control of the malignancy. In some hands, it has offered in a number of cases prolongation of life in some comfort.

Anus and Rectum: In anal and rectal malignant lesions, radon seed therapy has controlled the growth in many instances and in a few cases even offered a five-year cure. It certainly is a worthwhile procedure in operable cases and in early lesions which can be visualized through the proctoscope and when

surgical removal of the rectum is not acceptable to the patient. Its simplicity, ease of application, and ready control of dosage make this therapeutic method readily available for most rectal lesions. In rectal cases we have found seeds of 0.5-0.75 mcs. best for the purpose and less likely to cause local necrosis than seeds of larger strength. It is better to use seeds of lesser radioactivity at first and get an appreciable diminution of the lesion than to attempt complete destruction of the neoplasm with subsequent necrosis. Residual neoplasia can again be treated at a later date.

Gynecology: We have found radon seed therapy readily applicable in the treatment of localized vulvar, vaginal and urethral carcinomas. It is invaluable in the treatment of recurrent cervix lesions, especially with involvement in the fornices.

Genitourinary: In genito-urinary conditions radon seed therapy finds its most important application. Before 1900, treatment of genito-urinary conditions was essentially surgical. The invention of the cystoscope in 1878 made possible the subsequent development of intra-bladder irradiation with radon seeds. Duane's practical demonstration in 1914 that radium emanation could be piped into small tubules and Janeway's (3, 4, 5) recognition of the value of these findings led to the employment of radon seeds first by Barringer (6) in 1917, in the interstitial treatment of bladder and prostatic cancer through the operating cystoscope.

With improvement in technique and better control of radon content of seeds, effective results have been achieved, with definite relief to patients. Radon seed therapy is effective in treating malignancy of the scrotum, penis, bladder and prostate. Bladder lesions may be treated through the cystoscope or through a suprapubic cystotomy. Prostatic lesions may be treated by intratumoral seed implantation through the cystoscope, suprapubic cystotomy or through the perineal route.

An untoward concomitant effect of radiation, as heretofore carried out in the treatment of bladder cases, has been subsequent severe necrosis around the site of implanted seeds. This has been due to the excessive content of radon per seed as formerly prescribed. Barringer (7), in a clear-cut report based on a long and active experience, suggests that better results are being achieved by limiting the radon content of the seeds used in any case to 1-1.5 mc. per seed, thereby avoiding excessive dosage in a confined space and preventing excessive necrosis and secondary infection. We have found seeds of 0.5-0.75 mcs. of sufficient activity to produce good results. By observing these simple rules of using small content radon seeds more homogenously spaced, within a new growth and properly judging the dose required, good results should occur in most instances.

Orbit: Radon therapy has a definite place in the treatment of orbital tumors, especially in retinal gliomas.

Brain: In the treatment of brain tumors, radon seed therapy may be especially useful where removal of the neoplasm is impossible or only partially successful. Quick (8) in 1921 first reported on this treatment of glioma of the brain. Later, others gave more or less favorable reports; L. B. Rawlings in England, in 1932, reported on successful treatment of pituitary tumor with radon seeds.

Summary

Radon seed therapy is a rational method of applying irradiation to neoplasms throughout the body, especially to lesions in not readily accessible areas. Various technics for inserting radon seeds may be used and easily modified by requirements of the condition to be treated. The dosage can be accurately gauged. The residual metallic containers of radon have in no instances created any hazard when left remaining in the tissue. Loss of the seeds is of slight moment due to their insignificant value and their radioactivity is completely vitiated in thirty days.

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Jonathan Hutchinson, Man to Conjure With

A name to conjure with in our specialty is that of Jonathan Hutchinson, who was born in England in 1828, and who died in 1913. His interests in medicine were widely diversified. An opthalmic surgeon, a professor of clinical surgery, a dermatologist and syphilologist, he interpreted medicine and surgery on a broad basis. He described the Hutchinson triad in congenital syphilis. He described the first cases of infective angioma, or *infective nevus of Hutchinson.* He proposed the fish-eating theory of the causation of leprosy, and was the first to describe varicella gangrenosa. He independently described dysidrosis, later ascribed to Tilbury Fox. Hutchinson, who was sole contributor to the *Archives of Surgery* which he published, also described Hillard's lupus, or Mupus marginatus, and Mortimer's malady, a type of sarcoma. The names were chosen from the names of the patients involved. We also know the notched upper incisors of congenital syphilitics as *Hutchinson teeth,* and the Hydroa vacciniforme of Bazin was called *Hutchinson's disease,* despite the name he gave it of Recurrent Summer Eruption. Hutchinson was knighted in recognition of his work.

PREVENTIVE MENTAL MEDICINE

Preventive medicine, although more important than the treatment of illness, is and, by definition must be, more modest, less spectacular. Its effects are not clearly or immediately visible. They are cures before disease occurs, develops or establishes itself. All the teachings by a prevention-minded physician or by anybody else, resulting in the conservation of more health or in the avoidance of disease, constitute prophylactic work. So do, to a certain extent, the instructions leading to the resistance against possible complications. Sanitation belongs to the same class. The unassuming street cleaner, the garbage collector without any kind of a diploma, are also indispensable preventive agents.

Treatment, therapy, can say, "I have improved or healed the sickness", or, if not, "I have done my best". Cure may proclaim loudly and sensationally, "I have saved life, I have chased illness and brought back health". Credit is given them. But prevention can only claim to have avoided the trouble and indirectly the possible or probable catastrophe. This cannot always be proved, but the expert knows. He is convinced that what might have happened did not happen and his still voice tells him. "A stitch in time, an ounce of prevention".

Individual prevention in private practice is the same as public health on a huge scale, except that here statistics will show what has been done. Condemning the "lung blocks" in the slums, diminishing the working hours, improving the factories, educating the workers, has definitely prevented pulmonary tuberculosis and lessened its occurrence. The use of prophylactics has undoubtedly reduced the amount of venereal infection in the Army and Navy. Foreseeing an epidemic and taking measures beforehand, even if the work remains concealed from the public eye and unsung by the press, is better than fighting heroically afterward.

Prevention is similar to the man who has never taken and has always given, given of himself, and not like the philanthropist who first takes all he can and then gives conspicuously in spurts of grand display, cashing in gratitude, praise and honor.

Preventive *mental* medicine, wherever applicable, may be described in the same way.

The intelligent physician of the remotest past mixed mental preventive ideas with all his remedies. And the real success, not the one measured in pecuniary terms only, of the modern, scientific, enthusiastic doctor depends largely on how much mental health teaching his directions to the patient contain.

The courage lavishly imparted to the sick, the smile in the proper time, the frown in the right place, the conditional promise, the correct talk to the entire family, all this is mental hygiene, sown here and there, no matter what else is prescribed.

A few concrete examples of every day mental health prevention may not be amiss.

To the cardiac patient who believes that people with his ailment "drop dead in the street unexpectedly" the answer may be given that in such a form as this is newspaper gossip and that there is no real sudden death without some good reason, unless it is due to an accident. This allays his fear and cures part of his condition. Upon learning that he will not be permanently nailed to the bed and that he will soon be up and about, provided he follows the suggested measures, he is much helped. The humane doctor who speaks is regarded as a better physician than the one who is supercilious and mute and who just says: "Take this three times daily".

If you have only impressed upon your patient who, after a day's work, is spending most of his night playing cards, that sleep is extremely important, you have accomplished much. He came because of general debility and pallor. You have not cured him yet, but you have taught him how to live and given him the foundation for a cure. You have educated him that rest is essential and now he can use some of his time for a walk outdoors and for breathing some fresh air. The effect will be a better appetite for his food. You will also have improved his elimination and so have disintoxicated him. But what is more, you have calmed his fidgety nervous system and you may have prevented some sort of mental collapse.

You may not even always know the consequences of your preventive work. To have said to the middle aged store keeper to cut his day in two and lie down for an hour may not seem much. But it has steadied his afternoon, it has made him less grouchy and quarrelsome and has improved not only his business, but his mental health as well.

You have explained to a woman that her blood pressure was not dangerously high, that it is something changeable, that what she had learned from hearsay about it was all wrong, that she must leave it to you to estimate the pressure in relation to all her functions. She will be the healthier for that, both physically and mentally. And you have gained a friend.

A semi-neurotic is trying hard to convince you how sick he is, by disagreeably touching your shoulder, pointing to your chest and tracing his pain along your thigh. You hardly can stand his contact. But by listening to him with divine patience you find out, in addition to his physical symptoms, some of his home difficulties. Then you are of immense help to him because, while you ease his pains, real or imaginary, you cure him, in your conversations with him, of a possible psychosis before it can be recognized.

In another case the patient fails to speak because he regards everybody as untrustworthy. You succeed in gaining his confidence and you accomplish what amounts to a miracle. Where it was more difficult to extract a thought than to extract a tooth, you have done, as it were, a sort of mental surgery. You have made the patient talk to you, you have dimin-

ished his fears and you may be the only person who can keep him from falling into some mental trouble.

You see a woman slightly inclined to paranoia. She has "lost her voice", she complains, among other things. "Çara Nome" used to be nothing to me", she laments. Of course, you don't know anything about it. But judging from her general behavior, you cannot help doubting. But you succeed in convincing her about the value of her children, about their possible talents, about her share in promoting them. You may have saved her from a bad disorder before she went too far.

A not over-intelligent woman graduating rapidly into obesity was not only corporally uncomfortable, but also mentally despaired about her appearance. She had swallowed all possible medicines, was being mssaged and was taking gymnastic courses. However, she failed to do the one thing needful—eat less.

She said: "I'm trying hard to keep my old girlish shape." And your answer within yourself was: "You have more than succeeded, you have now a two-girl shape". She was quite depressed—which is not a paradox in many overweight persons. If you have listened to her story carefully and if you asked the right questions, you have surely discovered that there were some life problems connected with her condition.

You not only taught her how and how much to eat and how not to eat, but you also spoke to her husband and you have strengthened your conviction about the existence of a situation which encourages this overeating psychologically. Then you removed as much as possible of the mental cause and made her obey your instructions and you prevented a good many harmful possibilities.

You have attracted the parents' attention to their youngster's twitch of one eye-lid or to his nail-biting and you have had with them a talk about the child's temperament, about the question of upbringing, about various habit-forming imitations, including emotional seizures, like anger and, finally you have revealed to them the defects in their own behavior. Thus you have tapped some reservoirs which may have helped to prevent much maladjustment.

A patient who is ordinarily and in all respects well built is tortured by one obsession: his penis is "too small or shrunk"—which is quite a frequent complaint. Perhaps you can go to the bottom and uncover what forces him, deep down in his mind, to think that way or why he is so preoccupied with his organ. If not, if you can only persuade him, through any method, that he is wrong, he will get married and settle down and you will have saved an individual.

You may have to be stern and serious with him or superficial and humorous, according to circumstances. In one case the following true anecdote broke the spell: "My teacher of anatomy", said the doctor, "when I was a student, once described the penis and in all earnestness explained that in otherwise normal men this organ cannot be too small, but it does happen to be too large and then it is a distinct disadvantage and a bad handicap. The largest that has been observed in the world is now in London and I have the second largest—go up to our anatomical museum and you will see it."

Nor do we always deal with disease alone or with physical complaints only. The irreligious and wealthy children of an old little widow wanted the doctor, himself far from pious, to tell their mother that Church work and collecting used clothes for the means who was not free from a quiescent chronic kidney ailment.

The doctor knew her from the time he gathered data for his study on longevity and had questioned her as one of the persons over seventy. At that time she was already imbued with the ideas of justice and charity to which her family so strenuously objected. She constantly quoted Zola in his "Germinal": "Il faut rendre, il faut rendre". But now it was evident that her children, although providing for her financially, neglected her otherwise; that she had nothing else to live for than her benefactions, and that, for the sake of her mental state, this must absolutely be left to her. So the doctor, conspiring with this aged woman, helped her to a longer life and to continued happiness.

And so on and so forth.

65 West 95 Street

New Test Proves Worth of Senna

The tests on both laboratory animals and humans were completed at the Sterling-Winthrop Research Institute, Rensselaer, N. Y., and the first report on them was recently presented before the American Pharmaceutical Association, by Dr. Lloyd C. Miller, Director of the Institue's biology division.

Senna was introduced into medicine in the ninth century, according to Dr. Miller. It has been continuously used since then, chiefly in laxative preparations. Although the United States imports nearly 1,350,000 pounds of senna leaf annually for use in thousands of medical preparations, Dr. Miller declared that hitherto "no adequate attempt has been made to set up potency standards for any of the forms commonly seen in pharmaceutical commerce.

"Our investigations now prove that senna preparations can be assayed for potency on both mice and humans, and that mice can be used to determine the potency for human subjects", Dr. Miller reported. "In comparing nine different samples the results on the two species agreed well within the experimental error of the assay.

The potency of senna preparations may now be standardized and requirements may be established in official compendia".

Dr. Miller explained that the studies he conducted at the Institute "arose out of the necessity for determining the potency of senna preparations in connection with developmental work."

"The material under study consisted of experimental and commercial batches of proprietary preparations containing about 50 percent sugar and senna extractives equivalent to 50 to 100 mg. of fresh drug per cc," Dr. Miller reported.

To obtain dose-response data, Institute investigators used adult male white mice. In a typical experiment five groups of 22 mice each were set aside and each group received a different dose each test day. It was found that the responses fell into a normal pattern, so that conventional statistical techniques could be applied to calculate the results, and that the quantity necessary to produce a laxative effect in 50 percent of a group did not fluctuate significantly from day to day. Using this method for an assay procedure, the scientists determined that differences in potency of 20 percent could be readily picked up.

Having demonstrated that mice revealed differences in potency in preparations known to differ in age, method of manufacture, or actual senna content, experiments were conducted to test similar differences in humans, according to Dr. Miller. Each one of 28 subjects took six doses of three variants each of two different senna samples in the last experiment conducted. One sample was four-years old, the other fresh, and the potency calculations proved, Dr. Miller reported, to be in "almost incredibly good agreement with the results obtained on the same preparations in mice".

"This amazing concordance between assays on mice and men was observed in comparing two other preparations", Dr. Miller continued. "Of these two preparations, one was a commercial product and the other was prepared under laboratory conditions. It was found on mice that the potency of the commercial product was significantly less than the laboratory sample. Then an assay on 61 human volunteers was run, each of whom took two doses of both products, and it was found that the agreement between the humans and the mice is better than might be expected from the calculated standard errors."

Dr. Miller concluded that the application of these findings will make possible the establishment, without difficulty of specifications for potency of senna in its various pharmaceutical forms. If this is done, a reference standard senna will be needed. Data are in hand, demonstrating the feasibility of this course, which can be adopted by official regulatory bodies.

Dr. Bion East Receives New Appointment

The appointment of *Dr. Bion R. East,* prominent Columbia University faculty member, as chief of Veterans Administration Dental Service, was recently announced. Dr. East, who took over his new duties September 7, succeeds Dr. E. M. Kennedy, who has been acting chief of the Dental Service since the death of Dr. M. M. Fowler, October, 1947. Dr. Kennedy resumed his duties as head of the Dental Inpatient Service.

Dr. East is Associate Dean of the Faculty of Medicine, Executive Officer of the Department of Dentistry, and Professor of Dentistry at Columbia University, New York City. He also is chairman of the University Committee on Dental Education. He has been granted an indefinite leave of absence by the university to assist in VA's program of providing dental care for eligible veterans.

Dr. East is a Fellow of the American Association for the Advancement of Science and of the American Public Health Association. He is a member of the American Dental Association, the Michigan State Dental Association, the Detroit Dental Society, the International Association for Dental Research and the Public Health Association of New York.

Editorials

Golden Anniversary of New York City

The Medical Record was old when the five boroughs of the present Greater New York City joined in 1898. The offices of the ***The Medical Record*** had occupied space along lower Fifth Avenue; and had been on Park Place. Another address was on Vesey Street. These names of an older New York deserve a thought for a moment. How did they come to be so named?

Of course the system of numerical naming of the streets and avenues came after the old old New York moved north of Washington Square. Park Place was officially formed and named some time between 1831 and 1846. It was and remains a street west of Broadway to Church Street, later reaching the river. The site was once the location of Columbia College and had been the locale of another street, Robinson Street. This was in honor of a leading citizen of the New York about 1700 and was on the site of King's Farm ceded to King's College which later became Columbia College. One part of Robinson Street was known as College Place prior to 1846.

Vesey Street was so named about 1831 or earlier for Rev. William Vesey (1674-1746); first clergyman of Trinity Church beginning in 1697 and continuing in office to the close of his life half a century later. About 1698, Rev. Vesey married the widow, Mary Reade. Her husband, Laurence Reade for whom Reade Street is named was a leading merchant in the old city.

Some 300 named streets are located in lower Old New York. The origin of their names is shrouded in obscurity in all too many instances. A few are definitely known as eponymns (named after); others are guesses—some good, some bad—all too many just fairy tales. Romance, mystery, history, biography—all woven into named streets of Old New York on Manhattan Island!

One cannot refrain from submitting some few facts regarding the named.

The Collect, it is claimed, was once the site of an Indian Village. It was called Kalch-hook or shell point because of the collection of shells found on the shore of the Pond. The Kalch hook became abbreviated to Kacl or Colleck and then to Collect.

Ah, if the stones about Collect Pond could but speak?

And then yes, failure to know about Collect Pond resulted in tremendous additional cost in the preparation of the foundation of the present Tombs and Court Building on and near its site. The Older Tombs, too, showed the ill effect of the Pond. The building settled and settled over the decades—not evenly but in a manner causing cracks to appear in the masonry and plaster.

Broadway started as the Heere Wegh or Main street about 1643. It became variously known at different times for different stretches as Broadhighway, Great highway, Great Public road, Gentlemen's carriage road, Great Gentlemen's road, Great Broadway, and now Broadway.

In 1805, it was noted as the longest street in the City. Earlier at the time of the Declaration of Independence, Great George Street was the name of a section of Broadway from Fulton to Chamber's Street. Valentine's Manual in the 1850 and 1860 decades gave engravings of sections of Broadway. At one time, it was no farther north than in the seventies—until there the Broadway runs diagonally across the town, or so it seems. North of about 79th street, Broadway runs north and south more or less as do the other avenues.

Canal Street was a prominade along the forty foot canal at the northern boundary of the city. It was lined by trees. A bridge crossed the Broadway at Canal Street pictured in Valentine's Manual of 1857.

The Bowery is usually given as coming from the Bouwerie of Peter Stuyvesant, his country farm or home at Third avenue and 13th Street. This had a path leading to the City known as Bowery Lane, or Bowery Road and latterly as The Bowery. Its junction with Broadway is shown in Valentine's Manual as early as 1853 and for many years in the 1860 decade.

Chambers Street is said to have been ground originally King's land belonging to Trinity Church. The name has been claimed to come from John Chambers, Esq., a native New Yorker, successful lawyer, officer of Trinity Church, an official of the municipality, a member of the Provincial Council and Second Judge of the Supreme Court, 1751. In 1732, John Chambers leased some public lands. He married Anna van Courtlandt in 1737. At his death in 1774, it was reported he left a huge fortune.

MEDICAL RECORD

A National Review of Medicine and Surgery, Established 1843

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OCTOBER, 1948

Pearl Street is said to be the oldest street in New Amsterdam. It owed its name to the oyster shells along its path. Pearl Street was most fashionable. It was the favorite street along the East River. One section in 1695 was known as Great Queen Street. Another section from Wall to William Street was Hoogh Straat or High Street. Pearl Street is unique for it runs north and south and east and west in this City.

Catherine Street was named for Catherine DesBrosses.

Leonard Street was named for one of the three sons of Anthony Lispenard. Anthony, now Worth Street, and Thomas Street (one of the private streets of the City) were named for the other two sons.

Franklin Street was formerly Provost Street. It was named for Dr. Benjamin Franklin (1706-1790) the first civilized American. Franklin Square by the by was formerly St. George's Square. A Franklin Place and a Franklin Terrace are also known to New Yorkers of the era 1846-1882.

Roosevelt Street was named for Nicholas J. Roosevelt (1767-1854) according to The Olden Times Old New York of W. W. Pasko, 1890. Nicholas J. Roosevelt was associated with Robert Fulton.

Frankfort Street was named by Jacob Leisler for his home town, Frankfort, Germany. Leisler led the insurrection of 1690, was tried for treason and hanged, 1691.

Spruce Street is one of the streets named for varieties of trees. We have Elm (now Elk); Pine; Oak and others. Did these trees grow in the City?

Ann Street was named for Ann White, wife of Thomas White, prominent merchant and landowner. White Street is named for him.

Nassau Street is a very old street but it was named much later in honor of the princely house of Orange-Nassau.

The habit and manner of the practice of medicine in those old time New York streets has been given in a number of excellent biographies and not a few novels. The best is that of Samuel Bard of the first category and With Candle and Clock in the novel series.

Editorial

An introductory editorial is a dangerous thing. It's a golden opportunity for new ownership to make rash, high-toned promises. Comes the dawn following a few issues and the wordy, world-beating opener backfires. The readers, having given the publishers an even break on their initial promises, are disillusioned and disgusted.

So, picking our way carefully, we want to voice our aims, our hopes for the future . . . not rash promises but hopes, which are to become reality through conscientious and ambitious journalism.

MEDICAL RECORD is a fine magazine. It bears 105 years of proud tradition, a tradition that we shall work to carry on. We want to make it an even finer magazine. We shall do all in our power to put it at the top of the list of those magazines that serve the medical profession. To all who serve the world through medicine we shall try to bring a truly valuable offering of medical knowledge. We shall bring you each month articles by outstanding men in the profession, news of the medical world, and all material that furthers the progress of medicine today.

These are not idle promises. They are the basis upon which we begin publication of MEDICAL RECORD.

Leonard Martin Fox—Sol Shulman
Publishers

New Products

Miniature Batteries Manufactured by Hearing Aid Division

The Hearing Aid Division, Miniature Batteries, Sycamore, Ill., announced a new re-chargeable hearing aid battery—a wet-cell A battery offering up to 18 hours of heavy service with one charge, and thus offering the user greater battery economy, finer hearing aid performance, greater convenience.

The battery charges in six hours to full strength, using miniature charger plugged into regular AC outlet. It provides A battery service for an average cost of less than 1c per day, and eliminates the need for frequent changing, storage and rotating of conventional A batteries.

The new miniature battery weighs only 5 ounces, is fully contained in a plastic case measuring 1¼" x ⅞" x 3¾", and fits any two unit hearing aid.

The complete unit—re-chargeable Miniature Battery, plastic case, charger, and accessories sells at $9.75 by mail only, and carries a positive money back guarantee.

The battery can be plugged into charger when the wearer retires, and will be fully charged when he or she awakens six or more hours later.

Drug Injection Aids Asthmatics In Surgery

Intravenous injection of small amounts of the newly developed drug Isuprel provides control of asthma under anesthetics, thus removing one of the surgical hazzards for patients suffering from this condition. Laryngospasm and acute bronchospasm suffered by patients while on the operating table sometimes prove fatal.

Doctors Ellin N. Cohen and Frederick Van Bergen report, in the *Bulletin* of the University of Minnesota Hospital and the Minnesota Medical Foundation, that Isuprel injections provide "complete relief throughout the surgical and post-operative periods". Initial dosages varied from 0.16 to 0.02 milligrams. Largest total dose was 0.068 milligrams. Rises in pulse rate and blood pressure was minimal in all cases.

Isuprel was introduced this year by Winthrop-Stearns Inc. Laboratory investigations were initiated by the then Frederick Stearns & Co. Division of Sterling Drug Inc., Detroit, and were completed by the Sterling-Winthrop Research Institute in Rensselaer. Dramatic relief in treatment of asthma using Isuprel was first reported in this country by Dr. Maurice S. Segal, of Boston City Hospital.

Winthrop-Stearns to Market Cartose

Winthrop-Stearns Inc., pharmaceutical manufacturers, entered the infant food preparation field in its marketing of Cartose, a refined carbohydrate. This product was originally introduced by H. W. Kinney & Sons, Inc., of Columbus, Ind.

In announcing this addition to the Winthrop-

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Stearns' line, Dr. Theodore G. Klumpp, president, emphasized that the company is already well represented in the field of infant medicines through such products as vitamins, Drisdol, Betaxin and Cantaxin.

Wyeth Announces New "Aqueous" Penicillin

A new form of injectible penicillin, Wycillin, which will greatly simplify its use by the medical profession and make it much more widely available in fighting pneumonia, venereal diseases and other bacterial maladies, was announced by Wyeth Incorporated. The new product is likely to obsolete other earlier forms of the war-born wonder antibiotic drug because it can be carried around safely in a physician's pocket, and in aqueous solution retains its potency for as much as seven days without refrigeration.

The new Wyeth product, so far as the public is concerned, will do away with the pain associated with the injection of earlier forms of penicillin, and also will eliminate the danger of embolisms which have resulted in some cases from the injection of oil-and-wax and oil suspension forms of the drug used widely up to this time.

The new product is a procaine penicillin which when suspended in sterile distilled water and injected into the muscles of a patient, will maintain effective blood levels for twenty-four

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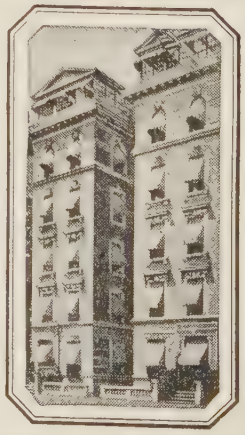

hours. The first successful dosage form of penicillin, still being used extensively, is the sodium salt of penicillin in dry form. Used in the same way as the new product, the original form had to be injected every three or four hours to accomplish the same result.

The next successful method, designed to avoid repeated injections, was the calcium salt of penicillin suspended in peanut oil and beeswax, developed by Captain Monroe Romansky, N. C. This preparation had several advantages over the original sodium salt because an injection of one cubic centimeter of the suspension containing 300,000 units of penicillin was needed only once in 24 hours, on the average, to maintain effective blood levels.

Wycillin is supplied in dry form, as was the original penicillin sodium. When sterile distilled water or normal saline solution is added, it provides procaine penicillin in a smooth, homogeneous suspension in water that can be easily withdrawn from a bottle and injected into the patient. The presence in the product of an innocuous suspending agent maintains even dispersement of the penicillin when in aqueous suspension. Like procaine penicillin with oil, Wycillin will provide effective blood levels for twenty-four hours.

Among its advantages is that the Wycillin aqueous suspension can be injected without pain to the patient, by avoiding the use of oil as a suspending agent. It also avoids the necessity for using a bone dry syringe.

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Book Review

Cerebral Palsy

Help Them Help Themselves. By JULIETTE MCINTOSH GRATKE, published by Texas Society for Crippled Children, Dallas, Tex. 1947.

It is heartening to see a general awakening of public interest in cerebral palsy. This condition, popularly but somewhat misleadingly known as "spastic paralysis", is seriously crippling disabling in its effects, and it is far more common than has been appreciated. There are approximately as many cases of cerebral palsy in this country as there are cases of infantile paralysis. The knowledge of this fact, together with the knowledge about cerebral palsy which Mrs. Gratke's book sets forth so clearly, should go far to quicken the public conscience with regard to the thousands of children who need and are not receiving the help which modern science and teaching are making available to the cerebral palsied.

This help must begin in the home and it must center in the home, if the cerebral palsied child is to have an essentially normal family environment. As Mrs. Gratke emphasizes, such an environment is of the greatest importance in determining the success of the program of care and training for a cerebral palsied child. The unique and very great value of Mrs. Gratke's long-awaited book lies precisely in the comprehensive and detailed consideration which it gives to the part which the cerebral palsied child's parents and family can and must play in providing the understanding and challenging atmosphere and the day-to-day care and training which every cerebral palsied child so urgently needs.

The book is filled to an impressive degree with the kind of detail and practical wisdom that could come only from the mother of a cerebral palsied child, a mother who, moreover, has undergone post-graduate training in speech pathology and other areas of specialized study in order to prepare herself for professional work with the cerebral palsied.

This sound and practical book should be placed in the hands of every parent of a cerebral palsied child, and it should be made available to all teachers, nurses, physicians, psychologists, speech correctionists, physiotherapists and others who are concerned with the welfare and training of the cerebral palsied. Mrs. Gratke has done a great service to a large and most worthy group of handicapped persons and to all those who minister to their needs and aspirations.

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Personals

Earle H. Daniel, formerly Prosthetic Specialist for the Medical Rehabilitation Division of the Veteran's Administration, Washington, D. C., has been appointed Chief of the Prosthetic Service, Institute of Rehabilitation, New York University-Bellevue Medical Center.

Mr. Daniel, himself an amputee, has been for the past 37 years an active figure in the development of medical rehabilitation for amputees. He is chairman of the Committee on Prosthetic Devices of the National Rehabilitation Council, consultant to the Division of Procurement of Prosthetic Devices of the United Nations and amputee consultant of the United Mine Workers, C. I. O. His wife, *Mrs. Helen H. Daniel,* will be his assistant in the new Institute post.

In cooperation with the medical staff of the Institute, the Prosthetic Service will sponsor a program of care, teaching and research, designed to aid in the development of the most modern practices and techniques for amputees. The new service provides a consultation department where doctors may send amputees to receive a prescription for artificial limbs, reference to appropriate manufacturers, adjustments and revisions needed to continue wearing finished limbs and training in the use of such limbs. The available equipment includes every known type of artificial limb, arm, hand and hook, and special machinery to make revisions.

The research program includes development of such devices as a "below the knee" limb for persons with amputations above the knee which allows them to have knee action and suction attaching devices for persons with facilities formerly thought inadequate for any type of artificial limb.

The new service will provide teaching facilities for New York University College of Medicine, the first medical school in the country to have established a Department of Rehabilitation as part of the regular course for undergraduates. Dr. Rusk is Professor of Rehabilitation and Chairman of the Department. In addition, graduate students and physicians from many parts of the country have already applied for postgraduate instruction.

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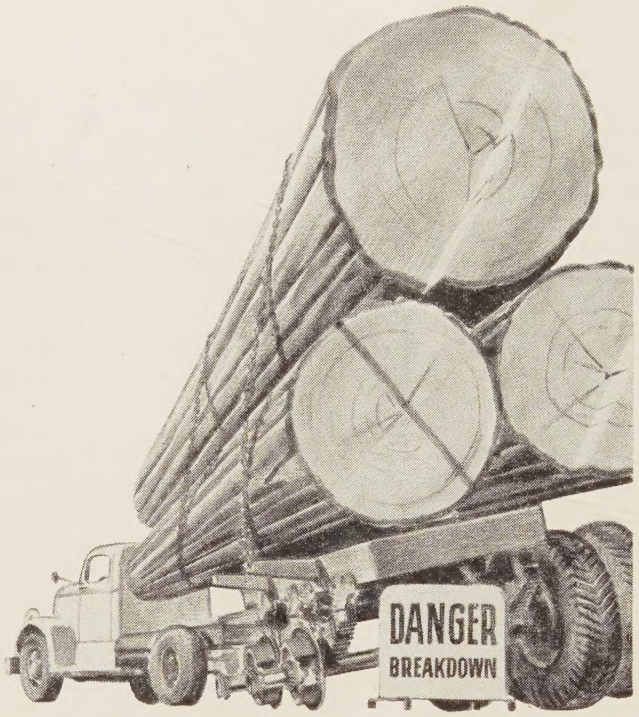

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Dr. Alfred H. Lawton, dean of the School of Medicine, University of North Dakota, Grand Forks, has been appointed chief of general medical research in the Veterans Administration Department of Medicine and Surgery.

In his new position, Dr. Lawton is supervising studies of epilepsy, psychoneuroses, hepatitis, peripheral nerve injuries and many other such diseases and wounds suffered by veterans. He succeeds Dr. L. G. Welt, who resigned to return to the Department of Internal Medicine at Yale University Medical School, New Haven, Conn., after nearly two years with VA.

Dr. Lawton was a research fellow in physiology and pharmacology at Northwestern, and has also been an assistant professor of medicine and of physiology and pharmacology in the Medical School of the University of Arkansas. Since 1947 he has been dean and professor of physiology and pharmacology in the Medical School of the University of North Dakota.

Dr. C. B. Spruit of the Veterans Administration Department of Medicine and Surgery in Washington, D. C., has been awarded an honorary degree as doctor of science by Illinois College, Jacksonville, Ill.

Dr. Spruit joined the Army Medical Corps in 1917 and served until October 1946, when he retired with the rank of brigadier general. During World War I, he served with U. S. forces in Siberia. Between the wars he served in Hawaii at the Army's Medical Field Service School, in the Surgeon General's office, and on the General staff.

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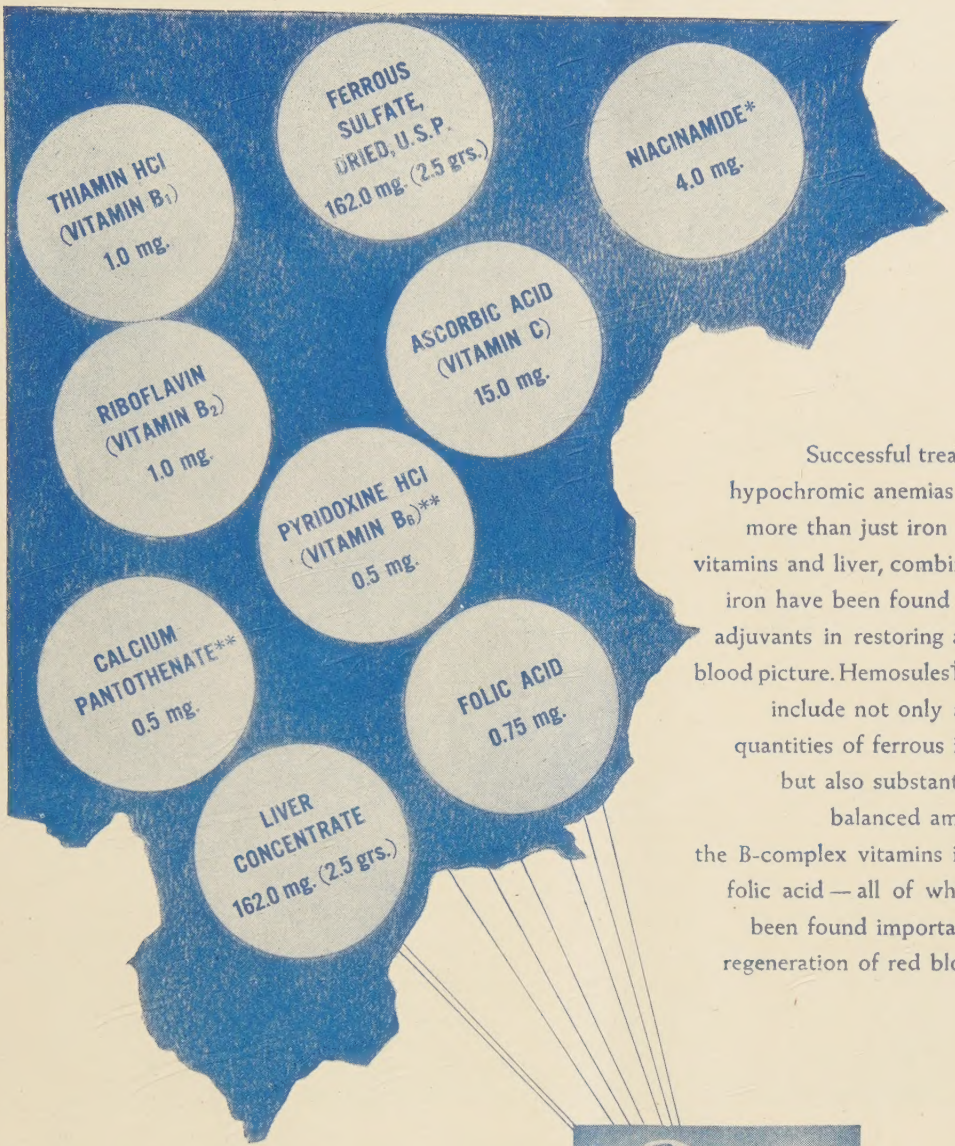
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PPO

Procaine Penicillin in Oil

For long-sustained blood levels with fewer injections and a minimum of the undesirable reactions inherent in the older, wax-containing preparations. One 1-cc. injection of 300,000 units of Heyden's thixotropic Crystalline Procaine Penicillin G in Sesame Oil yields effective penicillin blood concentrations for 24 or perhaps even up to 96 hours. A product of exceptional uniformity and pharmaceutical elegance, it is freely syringeable through an 18-gauge needle. The reliability and safety of Heyden's P P O were thoroughly established by careful clinical trials before its release for general medical use.

Available through your regular dealer.

We are now completing clinical studies on a companion product—Crystalline Procaine Penicillin G for Aqueous Suspension. It will soon be available and, like all Heyden penicillin products, worthy of your complete confidence.

FINE HEYDEN CHEMICALS

HEYDEN CHEMICAL CORPORATION

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